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SELECTION OF COLOR VISION TESTS FOR THE ARMY AIR FORCES

A Summary of Studies Made at the Army Air Forces School of Aviation Medicine

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SINCE the establishment of the Research Section of the Army Air Forces School of Aviation Medicine in December 1941, research on color vision has been one of the major projects of the department of ophthalmology. The primary purpose of these studies was to select tests for deficiency in red-green color vision which would be suitable for use in the selection of air force personnel. The material covered in this review is based principally on investigations carried out at the Army Air Forces School of Aviation Medicine between June 1942 and June 1945.

At the time these studies were initiated, four tests of color vision were authorized for use in the Army Air Forces: two basic tests and two adjunct tests.[1] The basic tests were the Ishihara test (eighth edition) and the American Optical Company Pseudo-Isochromatic Plates. The criterion of passing for both tests was that not more than 25 per cent of the plates be read incorrectly. It is not clear whether the decision to allow errors on a small number of plates was made with the idea that it would qualify men with only mild defects in color vision or because it was recognized that subjects with normal color vision read some of the charts incorrectly. A study of the adequacy

From the Army Air Forces School of Aviation Medicine.

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1. Wallace, S. R., Jr., and Rowland, L. S.: The Present Status of Color Vision Testing in the Army Air Forces, Report on File at Research Library, AAF School of Aviation Medicine, Randolph Field, Texas, March 29, 1944. Because of Civil Service Regulations, the second author's married name was used in the reports from the School of Aviation Medicine. Articles in journals are signed "Louise L. Sloan."

2. Rowland, L. S., and Heagan, F. V.: Frequency of Color Deficiency Among Air Corps Cadets, AAF School of Aviation Medicine, Project no. 314, Report no. 1, Randolph Field, Texas, Aug. 31, 1944.

of the basic tests as actually administered in the Army Air Forces [2] revealed that approximately one-half the subjects with deficient color vision remained undetected in repeated examinations. A similar study of the efficiency of the same tests as administered in the Navy [3] revealed the same percentage of candidates undetected with deficiency in color vision and revealed essentially the same factors to be responsible for failure to detect the defect.

The two adjunct tests authorized by the regulations were the Holmgren wool test and the School of Aviation Medicine lantern test. Ability to pass these tests was used to qualify men as "color safe" under certain conditions. Qualification for certain aircrew tasks was also made on the basis of the subject's ability to "distinguish and identify without confusion the color of an object, substance, material, or light that is uniformly colored a vivid red, and of an object, substance, material, or light that is uniformly colored a vivid green." The regulation gave no further information; consequently, it was left to the individual examiner to select a test and devise a method of scoring it so as to distinguish between those who did and those who did not meet this criterion. The wording of the regulation suggests, however, that its intention was to disqualify only those with complete red-green vision deficiency.

It is obvious that these color vision requirements are completely arbitrary. An analysis of available information regarding the color discriminations required of air crew, combat crew and ground crew members was needed to determine first whether normal color vision is essential for all such tasks. If not, and if a certain degree of deficiency in color vision can be permitted for certain tasks, then it is obvious that there is need not only for tests to distinguish subjects with normal from those with deficient color vision but also for tests which will measure the degree of deficiency.

The logical requirements for a thorough study of this problem can be outlined as follows:

(*a*) A "job analysis" to determine the type of color discrimination required of aircrew personnel, for example, pilots, navigators, bombardiers, gunners and radio operators; and ground crew personnel, for example, control tower operators, engineers and truck drivers.

(*b*) An evaluation of the already available tests for red-green color discrimination from the following points of view: (1) suitability as a screening test to distinguish between normal and deficient color vision or as a quantitative test for degree of defect; (2) reproducibility of

3. Farnsworth, D., and Reed, J. D.: A Survey of Methods Used in Administering Pseudo-Isochromatic Test Plates for Color Vision, Medical Research Laboratory, New London, Conn., Color Vision Report no. 3, Nov. 6, 1943.

the results in successive tests with respect to classification as normal or deficient color discrimination or with respect to degree of defect if color vision is deficient; (3) time required for administration and scoring of test; (4) possibility that applicants with deficient color vision might be coached to pass the test; (5) probability that scores on the test will be related to performance in color discriminations required in practice.

(*c*) The development and standardization of new tests if those already available are inadequate.

(*d*) Validation studies of the relationship between scores on various selected tests and performance in field tests simulating actual situations.

(*e*) From the results obtained in (*d*), selection of the most satisfactory test or tests and adoption of critical qualifying scores for various jobs.

The various lines of investigation summarized here were not actually carried out in the exact order given but were conducted more or less simultaneously, since it was necessary to adapt the conditions of the study to the facilities available and to study different aspects of the problem at the time that the particular tests, subjects, etc., were available.

ANALYSIS OF COLOR DISCRIMINATIONS REQUIRED OF AIRCREW PERSONNEL

The various types of color discrimination which may be of importance for aircrew personnel may be summarized as follows:

1. *Identification of Colored Light Signals.*—With the exception of the pyrotechnic type, all colored light signals are obtained from light sources combined with suitable color filters. Glide path indicators, traffic control projectors, airport beacons and identification and navigation lights on the plane are examples. The colors used for such lights are selected so as to be of high purity and to differ widely from one another in dominant wavelength. The pyrotechnic signals, owing to the greater difficulties in production and standardization of the colors, may differ less in dominant wavelength and may be of lower purity. The various colored light signals when viewed from a distance approximate point sources whose effective intensity decreases with the square of the distance. Consequently, even though objectively they differ widely in dominant wavelength and are of high purity, when seen from great distances or through fog or smoke, they may be difficult to distinguish because of the low intensity and the small visual angle subtended. They are also much more difficult to distinguish in the daytime, against the bright background of the sky, than when seen

against the night sky or other dark background. The person with deficient color discrimination may have greater difficulty than the normal person in detecting dim red lights, and he is likely to confuse red and amber, and green and white lights. It should be remembered, however, that the white lights are almost invariably of higher intensity than the green lights, and when both are present the difference in brightness may provide an auxiliary clue.

2. *Identification of the Colors of Various Reflecting Surfaces Used as Daytime Signals.*—This group includes flags, panels, colored "shapes" (balls, triangles, pyramids and cones), vehicles painted in certain colors for the purpose of identification and colored smokes. With the possible exception of the smoke signals, these colors are also of high purity and differ widely in dominant wavelength. Such signals may become difficult to detect, and the different colors may be difficult to distinguish from one another because of the decrease in the visual angle subtended when they are viewed from a great distance, or because of decrease in the intensity, owing to such factors as atmospheric conditions. The colored cones, balls, triangles and pyramids used as signals as a rule are of specific shape for each color, so that identification may be possible even when the color is not distinguished.

3. *Identification of the Colors Used for Coding of Equipment.*—Color coding is used, for example, to aid in the identification of fuel lines, oxygen lines and other aircraft piping. The colors used are red, yellow, white, green, blue, brown and black, in various combinations. Similar colors are used on gas cylinders. Identifying colors are also used for electric wires and fuses. The various colors used for coding are selected so as to show well marked differences. Special circumstances, such as dirt which obscures the colors, poor illumination or a small visual angle, may, however, increase the difficulty of identification by means of color. In many cases, clues other than color may be utilized. It is often possible to make the necessary identification of aircraft piping by means of differences in diameter, for example. The contents of gas cylinders are labeled in large white letters. Electric wires may be distinguished in some cases by diameter, by the presence or absence of marker threads or by attached tabs bearing distinguishing numbers. A continuity tester is also frequently used in tracing wires.

4. *Map Reading.*—Varying shades of tan and green are employed in navigation maps to indicate elevation. The elevations of greatest importance are, however, always indicated by figures printed in black.

5. *Color Differences in Terrain, Both Natural and Camouflaged.*—Various types of terrain, such as ploughed fields, sand, smooth grass

fields and swampy land, show differences in hue, in saturation and in brightness. Imperfectly camouflaged objects may differ from their backgrounds in a similar manner. Hendley and Hecht [4] measured the colors of natural objects and terrains. The colors were matched by direct comparison with the standard color chips in the Munsell Book of Color. The average color of forests, viewed from a distance of 1 or 2 miles (1,500 or 3,000 meters), was found, for example, to be 8.7 green-yellow in hue, 3.0 in value (brightness) and 1.5 in chroma (saturation). The color of distant objects "seen from two or more miles" was reported by them as 2.2 purple-blue in hue, 6.2 in value and 1.0 in chroma. According to these investigators,

> . . . because of the loss of saturation of distant objects, even the normal observer relies on brightness contrast for the principal clues in distinguishing objects at large distances. . . . In hazy weather, all color may be lost when an object is viewed from as little as ¼ of a mile.

Hendley and Hecht's measurements were made from the ground. In similar observations from a plane at high altitudes little loss in chroma was noted.[5] The differences in the results of the latter study are probably to be attributed to the greater clarity of the intervening atmosphere when one is looking directly downward from a plane.

The special difficulties experienced by subjects with defective red-green color vision in identifying terrain have perhaps been overemphasized. It is frequently stated that such a subject will be unable to distinguish the blue-green color of swampy terrain from the yellow-green of a grass field. A moment's thought will show, however, that this particular situation involves discrimination of yellow and blue, not red and green. It should be emphasized that, even though differences in hue and saturation in different types of terrain may be slight, differences in "texture" or brightness are usually well marked. Relatively smooth surfaces, for example, reflect much more light than areas with thicker growth. In the technic of camouflage, the great emphasis on accurate control of "texture," shape and shadows, and the fact that photographs in black and white frequently provide as much information as does direct visual observation are further indications of the greater importance of differences in brightness than in those of chromaticity (hue and saturation).

In order to obtain further evidence on this point, a member of the Central Instructors School at Randolph Field, Texas, was asked

4. Hendley, C. D., and Hecht, S.: The Colors of Natural Objects and Terrains and Their Relation to Visual Color Deficiency, Office of Scientific Research and Development, Report no. 269, February 1944.

5. History, Organization and Research Activities, Section V A, Color Vision, Staff Psychological Test Film Unit, Psychol. Bull. **41**:457-468 (July) 1944 (p. 464).

to make a flight wearing red "dark adapter" goggles and to report any difficulties in judging the nature of the terrain. Although wearing of such goggles does not simulate deficiency in red-green color discrimination, it does effectively remove all differences in hue and may also distort the brightness differences slightly. The pilot, nevertheless, experienced no difficulty in identifying ploughed fields, various types of grass fields, etc., or in selecting suitable terrain for a forced landing. While this simple experiment was not extensive enough to be conclusive, it again indicates that in the case of natural terrain brightness differences alone may provide entirely adequate information as to its nature.

There have been occasional reports of persons with deficient color vision said to be actually superior to normal persons in the detection of camouflaged areas. In order to investigate this possibility, an experimental study was made by Wallace and associates[6] on the comparative efficiency of subjects with normal and subjects with deficient color vision in detecting panels painted with camouflage colors, when these were laid flat on the ground so as not to provide clues due to shadows, and the like. The results for the entire group revealed a definite relationship of number of errors to brightness difference between panel and background but no similar relation for differences in hue. The 10 subjects with deficient color vision, 3 of whom had dichromatic vision, were definitely, though only slightly, inferior to the subjects with normal color vision. The "average number of errors per run" for the normal group ranged from about 2.3 to 3, and that for the subjects with deficient color vision, from about 2.6 to 4.1. It is concluded in this report that the slight difference between the performance of subjects with normal color vision and that of subjects with deficient color vision may be of no practical significance, since under actual conditions the latter could make use of auxiliary clues, such as shadows, not present in the experimental situation.

In considering the types of color discrimination discussed here, it should be remembered that conditions differ in combat and in noncombat areas and vary with the type of duty involved. In drawing any conclusions as to the special handicap of the subject with defective red-green color vision in making these discriminations the possibility of auxiliary clues must be kept in mind. It should be remembered, also, that about three fourths of the group with deficient color vision have only partial defects for red and green discrimination, which

6. Wallace, S. R.; Hexler, P. L., and Hecht, S.: Color Vision and Its Relation to the Detection of Camouflage, AAF Training Command Research Bulletin Hq. 43-6, Oct. 14, 1943.

are of varying degrees of severity. For these reasons it cannot be dogmatically concluded that all persons with deficient color vision should be disqualified for any particular duty, such as that of a pilot or gunner. For the greatest efficiency in the selection of personnel, therefore, a quantitative test of color vision is needed which will classify persons with deficient color discrimination as to the degree of the defect.

An analysis of the type of color discriminations involved is of value in indicating what types of test may be expected to be most closely related to actual performance. It was found that the color discriminations fall into two more or less distinct categories: (*a*) There are those in which, objectively considered, the colors differ greatly in chromaticity but subjectively may be difficult to discriminate because of low intensity or small visual angle or both. Most of the colored light signals, the colored reflecting surfaces and the colors used in coding of equipment fall in this first group; (*b*) in the second category are the discriminations in which the colors involved are of low purity and differ only slightly in dominant wavelength but are in most cases of fairly high brightness and large area. The colors of the terrain are the best example of this type of discrimination. Colored smokes and map colors may also fall into this second category.

Ability to perform the color discriminations included in the first category may be expected to be most closely related to high scores in tests employing colors of high purity but of low intensity and small area. The discriminations in the second category, on the other hand, will probably be most closely simulated by tests which measure discrimination of hue or saturation for colors of low purity but of high intensity and large area. As will be seen in later sections of this paper, these facts were kept in mind in the selection of the battery of color vision tests investigated.

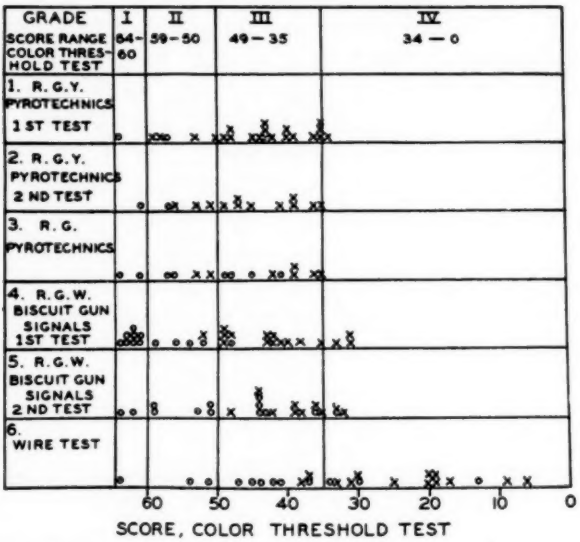
SELECTION OF TESTS FOR DETECTION OF AN ANOMALY IN RED-GREEN COLOR VISION AND FOR MEASUREMENT OF THE DEGREE OF THE DEFECT

A number of the available tests were investigated, and, where indicated, modifications were made in these tests. In addition, certain new tests have been developed for use in this study.

American Optical Company Pseudo-Isochromatic Plates.—The series published by the American Optical Company consists of 46 plates, copied in some cases from the Ishihara series and in other cases from the Stilling series. The American Optical Company test, until December 1944 one of the official tests in use in the Army Air Forces, was found to be unsatisfactory in several respects. Some of the charts taken from

the Stilling series have digits whose form is somewhat unfamiliar to American readers. Other charts are unsatisfactory because of poor reproduction of the colors of the original plates.

In the early part of 1942 a study was initiated at the Army Air Forces School of Aviation Medicine to determine whether a simpler and more reliable test could be obtained by the elimination of a number of the charts. It was hoped that such a test might at least serve until something better could be developed. Preliminary studies indicated that errors in reading certain of the charts are not necessarily indicative of deficiency in color vision, since they are made about as frequently by those who read a majority of the charts correctly as by those who fail in a majority. On the other hand, other charts are unsatisfactory



Relationship between scores on Color Threshold Tester and ability to pass various practical tests.

In this figure, *x* indicates failure to pass the practical test; *o* indicates that the subject passed the practical test. *R.G.Y.* indicates red, green and yellow; *R.G.*, red and green, and *R.G.W.*, red, green and white signals.

because they are frequently read correctly by those who fail in a majority of the charts.

Seventeen charts were selected which showed the highest consistency with the results obtained from the whole series. The abridged version recommended for adoption included 17 charts and 2 demonstration charts. In order to provide fewer clues for memorization, the charts were mounted on separate pages, so that they could be shown one at a time.

Similar studies were reported in the same year by Gallagher, Gallagher and Sloane.[7] The Royal Canadian Air Force [8] also proposed an abridged version of the American Optical Company test which consisted of 12 "essential" plates, used in diagnosing deficiency in color vision, combined with an additional 13 plates, which were not used in scoring. These were included in the series merely to make memorization more difficult. Selection of the 12 essential plates of the test used by Royal Canadian Air Force was based on its own data and those reported by the Army Air Forces School of Aviation Medicine and by Gallagher and associates. In 1944 the United States Navy issued for trial studies a new version of the American Optical Company charts. This series of 36 plates differs from the series recommended in the other investigations in that it is more than a mere selection of the better charts and incorporates several changes designed to increase the reliability of the test.

Rabkin Polychromatic Plates.—This test, published in Russia, is similar in principle to the Ishihara, Stilling and other tests using pseudo-isochromatic charts. Geometric figures, such as circles, squares and triangles, are employed, as well as digits. The configuration of the digits conforms closely to American usage. One special chart (no. 18) contains a number of green and brownish red squares, varying in brightness. Each horizontal row of squares contains either all green or all red squares. The brightness of the squares are so chosen that vertical rows of squares may be reported as of the same color by a person with defective color vision. Failure on this chart is probably indicative of a pronounced defect, since only a small per cent of the subjects with defective color vision make a definite selection of vertical rows when told to choose those containing squares of the same color. When the Rabkin test is used solely to differentiate subjects with normal from those with deficient color vision, considerable time is saved by the omission of this chart. In the present studies the two charts for detection of yellow-blue blindness were also omitted, since this type of defect is probably rare. The Rabkin test is difficult to obtain in this country at the present time. It was of particular value in this investigation as a check in doubtful cases, because there was no possibility that the subject could have been coached to pass this test.

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7. Gallagher, J. R.; Gallagher, C. D., and Sloane, A. E.: A Critical Evaluation of Pseudo-Isochromatic Plates and Suggestions for Testing Color Vision, Yale J. Biol. & Med. **15**:79-98 (Oct.) 1942.

8. Nicholls, J. V. V.: R.C.A.F. Colour Plate Test, Report to Associate Committee on Aviation Medical Research, National Research Council of Canada, Ottawa.

School of Aviation Medicine (S. A. M.) Anomaloscope.[9] — This instrument is a modification of the Eastman Color Temperature Meter. One-half a circular field is illuminated by yellow light, the other half, by a mixture of red and green, the proportions of which can be varied. The instrument is of conveniently small size and can be purchased for about $18. The substitution of another scale for the one graduated to read color temperature and the use of an auxiliary green filter to extend the range, although not absolutely essential, make the instrument more satisfactory for use as an anomaloscope. The test procedure used in these studies provides for three classifications: normal, moderately defective and markly defective color vision. Subjects having a moderate defect may be further classified as deuteranomalous or protanomalous in type. Further details regarding the instrument, procedure and results are given in reports from the School of Aviation Medicine.[9]

The Rand Anomaloscope (Bausch and Lomb).—This instrument is still in the developmental stage. An experimental model was available for a short time during the course of color vision studies at the School of Aviation Medicine. If a test procedure is employed similar to that used in the S. A. M. anomaloscope, two degrees of defect can also be distinguished by this test. A somewhat more elaborate test procedure can also be used, which may possibly provide finer classifications as to degree of defect.

Inter-Society Color Council (ISCC) Single Judgment Test.[10]—In this test the observer is presented with a pair of chips and is required to say which chip of the pair is redder. The series contains 10 pairs of red chips which differ in saturation by small steps and 10 pairs of purple-red chips. In the form in which the test was used at the School of Aviation Medicine, the 10 pairs composed of red chips are shown first, then the 10 pairs composed of purple-red chips. The whole series is then presented a second time with the position of the pairs reversed from right to left. The complete test, therefore, requires a total of

9. Rowland, L. S.: A Simple Anomaloscope for Detecting and Classifying Red-Green Color Deficiencies, AAF School of Aviation Medicine, Project no. 137, Report no. 2, Randolph Field, Texas, July 29, 1943; Further Studies with a Simple Anomaloscope for Detecting Red-Green Color Deficiencies, AAF School of Aviation Medicine, Project no. 137, Report no. 3, Randolph Field, Texas, Sept. 23, 1943. Dimmick, F. L.: A Portable Anomaloscope for Screening Color Deficiency, J. Optic. Soc. America **34**:352 (June) 1944. Sloan, L. L.: The Eastman Color Temperature Meter Used as an Anomaloscope, ibid. **34**:618-620 (Oct.) 1944.

10. Hardy, L.: Single Judgment Test for Red-Green Discrimination, J. Optic. Soc. America **33**:512-514 (Sept.) 1943.

40 judgments. Preliminary studies with this test[11] indicated that the scores were not sufficiently reproducible to warrant its use as a means of measuring degrees of color deficiency. It was further observed that some subjects with definitely deficient color vision were able to make perfect scores, probably because they made use of brightness rather than saturation differences and selected the darker chip as the redder. Studies made by various members of the ISCC committee indicated that the second difficulty might be obviated if they returned to the procedure previously used and presented the red and purple-red chips alternately in random order. No studies were made at the Army Air Forces School of Aviation Medicine using this procedure.

Eastman Hue Discrimination Test.—The essential principles of the test as used at the Army Air Forces School of Aviation Medicine may be described briefly. The test target consists of a yellow Landolt C on a green background. The target is superimposed on an evenly illuminated yellow-green "masking field." The test field seen by the subject, therefore, consists of a letter C composed of a mixture of yellow and yellow-green light, on a background composed of a mixture of green and yellow-green light. When the brightness of the masking field is much greater than that of the target, the letter and background will be yellow-greens differing only slightly in hue. The difference in hue is varied in fixed steps by variation in brightness of the masking field. The test consists in determining the smallest difference in hue at which the subject can report correctly the orientation of the letter C.

Thirty subjects with normal and 31 subjects with deficient color vision were tested with this instrument at the Army Air Forces School of Aviation Medicine. Some overlapping was found in the scores of the two groups. The few normal subjects who had as poor hue discrimination as some subjects with deficient color vision showed decided improvement on retests. The test requires high concentration of attention and maximum cooperation, and it is probable that normal subjects occasionally make poor scores owing to inattention. Several subjects with pronounced defects in color vision according to other tests showed relatively slight deviations from normal in this test. One of these men reported that he was able to detect the break in the C because it was lighter than the rest of the ring but could distinguish no difference in color. Another reported that the break was darker than the rest of the ring. In a test field of the type used in this instrument very small brightness differences are discriminable. Because of the difficulty of equating the brightness of the C and the background

11. Rowland, L. S.: An Evaluation of the ISCC Test for Color Deficiency in the Selection of Air Force Personnel, AAF School of Aviation Medicine, Project no. 54, Report no. 1, Randolph Field, Texas, May 29, 1942.

for all subjects with deficient color vision of both protanopic and deuteranopic types, it was concluded that further investigation of this test was not advisable.

Farnsworth-Munsell 100-Hue Test.[12]—The material used in this test consists of 85 color disks selected from a series of 100 Munsell papers which are equal in brightness and saturation but which vary in hue by small steps and cover the entire possible range of hues, i. e., reds, yellows, greens, blues and purples. The color disks are presented in four groups, containing about 20 colors each. The task of the subject is to arrange each group in a graded series, varying, for example, from red to yellow or from yellow to green.

The results are plotted on a special graph. If this graph indicates poor hue discrimination for blues varying from reddish blue to greenish blue and for yellows varying from greenish to reddish yellow then a deficiency in red-green color vision is indicated. The relatively rare cases of yellow-blue blindness are also revealed by this test. Subjects with this defect show poor hue discrimination for reds varying from bluish red to yellowish red and for greens varying from bluish to yellowish. Some subjects have poor hue discrimination which is not clearly localized in two regions of the hue circle. A majority of these show deficiency in red-green color vision on other tests. Considerable time is required to record, score and chart the results of this test. For this reason and because the results are sometimes difficult to classify as to type and degree of defect, the test was not used routinely in this investigation but was given only to certain subjects showing atypical responses on other tests.

Terrain Test.[13]—The material of Farnsworth's test was used in devising the terrain test. This was designed to simulate the hue discriminations involved in identification of the colors of natural terrain. For this purpose, alternate chips in the series were selected ranging from red to yellow-red to green to bluish green. A total of 20 chips was used. As in the original test, the task of the subject was to arrange these in consecutive order. A simpler scoring system than that used by Farnsworth was adopted. If all the chips are arranged by the subject in the proper sequence, the score is zero with this method of scoring. Interchange of two chips gives an error score of 1, and in general the magnitude of the score increases with the degree of deviation from the correct order. The range of hues chosen for the terrain test was

12. Farnsworth, D.: The Farnsworth-Munsell 100-Hue and Dichotomous Tests for Color Vision, J. Optic. Soc. America **33**:568-578 (Oct.) 1943.

13. Rowland, L. S.: Selection and Validation of Tests for Color Vision: A Test for Ability to Distinguish Terrain Colors, AAF School of Aviation Medicine, Project no. 137, Report no. 1, Randolph Field, Texas, May 31, 1943.

selected because it includes one of the two regions in which hue discrimination is poor for person with red-green color deficiency, and because the reds, yellows, greens and blue-greens used are representative of the colors of natural terrain. Further details with regard to the terrain test are given in the School of Aviation Medicine Report no. 1, project no. 137, May 31, 1943.

Peckham Color Vision Test.—This is a color-matching test using 20 Munsell colors which appear equal in brightness and saturation to the normal person (value 5, chroma 4). The colors represent equal hue intervals on the Munsell color scale. A mechanical system permits the 20 hues to be compared in random order with each of the five standard hues, red, yellow, green, blue and purple. The subject's task is to report which pairs appear to him a perfect match. The normal subject should report as matched the 5 pairs which are identical and may include also those pairs which differ by one step in hue. Red and red yellow-red or green and green yellow-green, for example, might be reported a perfect match by a subject with normal color vision. A few normal subjects fail to report the supposedly identical colors as matched, presumably because of slight differences in the illumination falling on the two samples. Those with a pronounced deficiency in color vision may report as perfect matches colors which differ widely in hue, for example red and green or red and blue-green. Many subjects with deficient color vision give responses which cannot de differentiated from normal. It is probable that even when the subject with deficient color vision fails to see a difference in hue, the colors may appear to him slightly different in saturation or in brightness. It is easy to simulate normal color vision in this test if the subject with deficient color discrimination knows that only a few pairs of colors should match. Because of these and other objections to the test, it was not included in the battery of tests retained for further study.

Tests of the Lantern Type.—Williams Lantern: A study of this instrument was made by Farnsworth and Reed.[14] They reported that the scores are difficult to interpret and correlate poorly with those for other tests and that the test does not distinguish observers with normal from those with moderately deficient color vision. Because of this unfavorable report, no study was made of this test at the School of Aviation Medicine.

Canadian Lanterns: The Royal Canadian Navy lantern employs red, green and white (actually yellow) test lights, subtending very small visual angles. Two test lights are shown at a time, and all

14. Farnsworth, D., and Reed, J. D.: Examination of the Williams Lantern as a Test for Color Vision, Medical Research Laboratory, New London, Conn., Color Vision Report no. 6, Nov. 22, 1943.

9 possible pairs are shown. The test lights are approximately equal in intensity, with the exception of one less intense white of the pair of white lights. Farnsworth and Reed [15] reported that the test is simple to administer and to score. According to them, its only disadvantages are that (1) it does not distinguish types or degrees of color deficiency, (2) it allows some subjects with slight defects to pass as normal, (3) it does not detect malingerers effectively and (4) it requires a dark room.

The Royal Canadian Air Force recommended a modification of this lantern in which amber test lights were used in addition to red, green and white. The "Canadian Lantern test" studied at the School of Aviation Medicine is essentially similar to the test proposed by the Royal Canadian Air Force.[16] The procedure and method of scoring adopted after preliminary experiments were those found to give the highest reproducibility of scores and the best differentiation of subjects with normal and deficient color vision.

Color Threshold Lantern [17]: This instrument was developed at the School of Aviation Medicine and differs from the Canadian and other lantern tests in several important respects. Each of the 8 test colors used is shown at 8 different intensities, the highest of which is approximately one hundred times the lowest. The minimum intensity differs for each color and is so chosen that a majority of subjects with normal color vision give the correct response at this level. At the lowest level of intensity the 8 test colors are therefore of approximately equal difficulty so far as recognition of the color is concerned. At the second level the intensities are double the minimum values, and at each succeeding level they are double those of the preceding one. The 8 colors are chosen so as to be representative of the permissible ranges for aviation colors. The 2 green test lights, for example, approximate the blue and yellow limits for aviation green. The method of scoring the test was selected so as to emphasize the difference in the responses of subjects with normal and with deficient color vision and so as to put a greater penalty on errors at high than at low levels of intensity.

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15. Farnsworth, D., and Reed, J. D.: Trial of Royal Canadian Navy Colour Lantern in Comparison with Other Tests of Color Vision, Medical Research Division, New London, Conn., Jan. 18, 1943.

16. Rowland, L. S.: Selection and Validation of Tests for Color Vision: A Comparison of Two Lantern Tests for Red-Green Deficiency, the Color Threshold Lantern and a Modification of the RCN (Royal Canadian Navy) Lantern, AAF School of Aviation Medicine, Project no. 137, Report no. 4, Randolph Field, Texas, Oct. 21, 1943.

17. Rowland, L. S.: Selection and Validation of Tests for Color Vision: The Color Threshold Lantern as a Quantitative Test for Red-Green Color Deficiency, AAF School of Aviation Medicine, Project no. 137, Report no. 5, Randolph Field, Texas, Oct. 20, 1943. Sloan, L. L.: A Quantitative Test for Measuring Degree of Red-Green Color Deficiency, Am. J. Ophth. **27**:941-947 (Sept.) 1944.

RESULTS OF INVESTIGATION

Screening Tests.—Of the various tests investigated, those of the anomaloscope type and those employing pseudoisochromatic charts appear to be particularly suitable for use as screening tests because they are simple and can be given rapidly and because the percentage of failure on such tests is higher than that on other types of test which were studied.

A study was made at the School of Aviation Medicine [18] in which the abridged American Optical Company test, the Rabkin test, and the S.A.M. anomaloscope test were compared as to their efficiency as dichotomous tests for distinguishing normal from deficient color percep-

TABLE 1.—*Results of Three Screening Tests of Color Vision*

Rabkin Test, Number Errors	Anomaloscope and Abridged A. O. C.* Tests		Abridged A. O. C. Test, Number Errors	Anomaloscope and Rabkin Tests		Anomaloscope Point of Reversal	Rabkin and Abridged A. O. C. Tests	
	Passed	Failed		Passed	Failed		Passed	Failed
0	68	0	0	64	0	0	49	5†
1	28	1†	1	25	0	±0.5	34	4†
2	1	0	2	6	0	±1.0	14	1†
..	..	..	3	2	4†	..	..	..
3	..	1	..	..	..	±1.5	0	4
4	..	1	4	2†	5	±2.0	0	9
5	..	6	5	1†	5	±2.5	1†	115
6	..	6	6	..	4	±3.0	..	93
7	..	6	7	..	10	±3.5	..	47
8	..	15	8	..	11	±4.0	..	9
9	..	17	9	..	10	±4.5	..	1
10	..	32	10	..	16	No point of reversal	..	101
11	..	58	11	..	18		—	—
12	..	136	12	..	17	Total.....	98	389
13	..	101	13	..	21			
	—	—	14	..	42			
Total....	97	380	15	..	48			
			16	..	72			
			17	..	100			
				—	—			
			Total.....	100	383			

* A.O.C. indicates American Optical Company.
† Nineteen subjects, indicated by daggers, gave inconsistent results on the three tests.

tion. The three color vision tests were scored according to the following standards:

1. Abridged American Optical Company test: 0 to 3 errors, pass; 4 to 17 errors, failure.

2. Rabkin test: 0 to 2 errors, pass; 3 to 13 errors, failure.

3. S.A.M. anomaloscope test: scores between + 1.0 and — 1.0, pass; outside these limits, failure. With these criteria, there is a close agreement in the classifications with the three tests. Of the 495 subjects tested, 379 failed all three tests; 97 passed all three tests, and 19 gave inconsistent results. The results are given in further detail in table 1.

18. Rowland, L. S.: An Abridged Edition of the American Optical Company Plates for Testing Color Perception: Comparison with Other Screening Tests, AAF School of Aviation Medicine, Project no. 68, Report no. 3, Randolph Field, Texas, May 8, 1945.

The occasional subject who does not show consistent evidence of deficient color vision on all three tests is of especial interest from a theoretic point of view. Such a subject should receive further study in order to provide information as to the causes of the discrepancy and to determine whether it is perhaps indicative of a slight deviation from normal. The available data on the 19 subjects of this type are given in table 2. The relatively high scores made by a majority of these subjects on the Color Threshold Test indicates that in at least one particular aspect of color discrimination they differed little from normal.

TABLE 2.—*Data on Nineteen Subjects Giving Inconsistent Results on Three Screening Tests of Color Vision*

Subject Number	Errors in Abridged A.O.C.* Test	Errors in Rabkin Test	Anomaloscope Point of Reversal	Score C.T.T.†	Comment
1	4	0	−0.5	Not determined	
2	4	0	0.0	Not determined	
3	5	2	−0.5	62	
4	3	2	+2.5	56	
5	3	8	+2.5	50	Subject probably memorized some A.O.C. charts
6	3	8	+2.5	48	Subject probably memorized some A.O.C. charts
7	3	4	+3.0	62	
8	3(?)	7	+3.5	57	On 6 A.O.C. charts of dual response type subject saw both numbers with equal clearness; no other errors
9	8	1	+3.5	62	
10	6	8	0.0	63	
11	7	3	0.0	63	Normal responses also on Rand anomaloscope; 5 errors in recheck on Rabkin test
12	8	8	0.0	63	Normal responses also on Rand anomaloscope; Farnsworth 100-Hue test shows definite defect
13	9	10	0.0	59	
14	9	7	+0.5	61	
15	11	8	0.0	63	Normal response also on Hecht anomaloscope
16	11	8	+1.0	57	Woman whose son also has deficient color vision
17	14	12	+0.5	40	
18	15	11	−0.5	50	
19	16	13	+0.5	64	

* A.O.C. indicates American Optical Company.
† C.T.T. indicates S.A.M. Color Threshold Test.

It may be concluded that any one of the three tests will serve as an efficient screening test, since, with rare exceptions, subjects who fail one also fail the other two tests and since the exceptional cases are found primarily among subjects who have only a slight deficiency in color vision. In selecting one of the three tests for adoption as a screening test, several considerations are of importance. At the present time the Rabkin test is not available in this country in sufficient quantity to supply all the Air Force installations which would require them. If this test became generally distributed, as has been the case with the standard Ishihara and the American Optical Company tests, it would be easy to coach subjects to give the correct answers, since the Rabkin charts are so constructed that there are many auxiliary clues for memorization. If knowledge of the charts composing the abridged

American Optical Company test becomes available to the general public, its reliability will also suffer. Methods for training subjects with deficient color vision which aid them in reading such charts have recently been advocated. Dvorine,[19] for example, has published two volumes of such charts, one for training and one for testing. He reported that training on the first set of charts enables many subjects to read the charts of the second set. It is conceivable that there is sufficient transfer of training with some subjects to enable them to read with greater facility not only the charts on the Dvorine series but also those in other pseudo-isochromatic tests. Even if this does occur, however, it does not indicate any real improvement in color discrimination, which will extend to situations in which the required color discriminations differ significantly from those involved in reading such charts.

The methods of training in use at the present time do not, however, appear to be successful enough to present any serious problem. A total of 22 men who had taken some form of training which involved study of the standard American Optical Company and the Ishihara charts have been examined at the School of Aviation Medicine. The number of errors made in reading the 17 plates of the abridged test were, respectively, 16, 15, 15, 14, 14, 14, 13, 13, 10, 9, 8, 8, 7, 6, 6, 6, 6, 5, 5, 4, 4, and 3. Although the previous training probably resulted in fewer errors, only 1 of the 22 men was able to make a passing score.

It seems less likely that applicants could easily be coached to give normal responses on the anomaloscope test. This test would be of value, therefore, as a supplementary test, to be given to applicants whose responses in the abridged American Optical Company test indicated a questionable or borderline defect. It could also be used from time to time in "spot checks" to make sure that the abridged American Optical Company test was being properly given and that knowledge of the charts had not been disseminated among the applicants.

Quantitative Tests.—The efficiency of a quantitative test of color vision to be used in the selection of aircrew personnel depends primarily on the reproducibility of the scores and the relationship of those scores to performance in the color discriminations actually required of such personnel.

The three tests evaluated in the previous section as possible screening tests also provide quantitative scores which could be used as an index of the degree of defect if shown to meet aforementioned criteria. Three other tests were extensively investigated in this study, the terrain test, the Canadian Lantern test and the Color Threshold Test. These tests

19. Dvorine, I.: A New Diagnostic Method of Testing and Training Color Perception, Am. J. Optometry & Arch. Am. Acad. Optometry **21**:225-235 (June) 1944.

are not suitable for screening purposes because they are time consuming and because they do not detect all subjects with deficient color vision. They could, however, be used in conjunction with a preliminary screening test to determine the degree of defect in subjects who fail the preliminary test.

A. Reproducibility: The two pseudoisochromatic chart tests show high reproducibility in the number of errors made in two independent tests. A study at the School of Aviation Medicine in which the results obtained with natural daylight illumination were compared with illumination from daylight fluorescent bulbs gave indirect evidence that the error score made by any subject is a relatively constant quanity.[20] No detailed studies of the reproducibility of the scores with the S.A.M. anomaloscope have been made. The Color Threshold Test, the Canadian Lantern test and the terrain test are in a sense performance tests rather than direct measures of color perception, and scores on these tests are in part determined by chance factors. It might be expected, therefore, that the scores would show a greater variation in successive tests. Actually, however, all three tests show a sufficient degree of reproducibility to warrant further study of their validity.

Studies at the School of Aviation Medicine [21] gave data on the test-retest correlation of the scores on the Color Threshold Test and the Canadian Lantern test. The subjects tested in that investigation included very few with pronounced defect; the correlation coefficients are, consequently, reduced by this limitation in range. Later data were, however, obtained for the Color Threshold Test based on a more representative range of defects. These data gave a test-retest correlation of 0.88 ($N = 94$) for two tests made on different days, the interval between tests varying from one week to as much as six months. The earlier studies, on subjects showing a more limited range of defects, gave a correlation coefficient of 0.80 for the Color Threshold Test and 0.62 for the Canadian Lantern test ($N = 43$). This difference, though not statistically significant for 43 cases, at least suggests a higher reliability for the Color Threshold Test. Use of the Pearson product moment formula to determine the reliability of the terrain test is not possible because the scores do not give a normal distribution. Data on 32 subjects (table 3) indicate that a scoring system for this test could be devised which would give a reliable measure of several degrees of color vision deficiency.

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20. Rowland, L. S.: Daylight Fluorescent Lamps as a Source of Illumination in Tests of Color Perception with Pseudo-Isochromatic Plates, AAF School of Aviation Medicine, Project no. 130, Report no. 1, Randolph Field, Texas, April 1, 1943.

21. Rowland (footnotes 16 and 17).

B. Validity: An investigation of the relationship between scores on a number of tests of color vision and ability to identify "biscuit gun" signals is reported in detail in School of Aviation Medicine Research Project no. 137, Report no. 7.[22] The six tests studied were the abridged American Optical Company Psuedo-Isochromatic Plates, the Rabkin Polychromatic Plates, the S.A.M. Anomaloscope, the terrain test, the modified Canadian Lantern test and the S.A.M. Color Threshold Test. Thirty-four subjects with normal and 84 subjects with deficient color vision took part in these experiments. The results indicated that only the last two tests gave scores which showed any relation to ability to identify biscuit gun signals and that the Color Threshold Test was

TABLE 3.—*Scores on the Terrain Test for Thirty-Two Subjects*

Scores		Scores		Scores	
First Test	Second Test	First Test	Second Test	First Test	Second Test
1	0	2	1	7	10
1	0	3	0	12	5
1	0	3	0	24	20
1	0	3	0	27	35
1	1	3	0	31	56
1	1	3	2	32	25
1	1	3	7	32	30
1	1	4	3	46	27
1	4	4	5	61	75
1	4	5	1	62	67
2	1	6	7		

the better of the two in differentiating between those who could and those who could not distinguish the biscuit gun signals correctly.

In a second study, the relationship between scores on the Color Threshold Test and ability to recognize colored pyrotechnic signals was investigated.[23] In a third study, not previously reported, the relationship between scores on the Color Threshold Test and ability to identify electric wires by means of the colors used in the coverings was investigated. A cable composed of 15 wires of 8 different colors was employed in these tests. One wire in the bundle was shown to the subject by separating it from the others for an instant. The subject was then

22. Rowland, L. S.: Selection and Validation of Tests for Color Vision: Relationship Between Degree of Color Deficiency and Ability to Identify Signals from a "Biscuit Gun," AAF School of Aviation Medicine, Project no. 137, Report no. 7, Randolph Field, Texas, Nov. 3, 1943.

23. Rowland L. S.: Selection and Validation of Tests for Color Vision: The Recognition of Pyrotechnic Signals by Normal and Color Deficient Subjects, AAF School of Aviation Medicine, Project no. 137, Report no. 6, Randolph Field, Texas, Nov. 1, 1945.

required to select this same wire from the complete bundle. Typical errors made by the subjects with deficient color vision were confusion of brown and red, blue and green, brown and green, and green and orange.

The relationships between scores on the Color Threshold Test and performance in the several practical tests are summarized in the accompanying chart. In this chart each cross or circle represents a subject with deficient color vision. Those who failed the particular practical test are indicated by crosses; those who passed, by circles. The location of the cross or circle on the horizintal meridian corresponds to the subject's score on the Color Threshold Tester. Inspection of the chart shows that discrimination of red, green and yellow pyrotechnic signals is a difficult task for the person with deficient color vision. No one with a score below 57 passed this test. Although a relatively small group took part in the tests in which only red and green pyrotechnics were used, the results suggest that the task is much easier for the subject with deficient color vision when yellow pyrotechnics are omitted. Of the 9 subjects making scores of 44 or higher, 7 passed this test.

In the first experiment with biscuit gun signals, 12 of the 13 subjects with scores above 50 passed the test, as compared with only 1 of the 16 subjects with scores below 50. The second test with biscuit gun signals does not show such a well marked differentiation. All those with scores above 50 passed, but a number with low scores also passed. A critical score of 50 would, therefore, not qualify men unable to discriminate red, green and yellow biscuit gun signals but would disqualify some who are able to do so. Identification of colored electric wires proved to be much easier than the identification of colored light signals. All subjects with scores above 40 and some with scores between 30 and 40 passed this test.

While the selection of qualifying scores for various tasks must be somewhat arbitrary until more extensive investigations are made, tentative critical scores provide the basis for distinguishing four grades of color deficiency in those who fail the pseudoisochromatic charts: grade 1, scores 64 to 60; grade 2, scores 59 to 50; grade 3, scores 49 to 35; grade 4, scores of 34 or less. The validating tests show that subjects with grade 4 scores make errors in identifying electric wires by color. Subjects with scores classified in grade 3 as a rule have only a partial defect for red and green. They are able to distinguish the colors of electric wires but will make errors in distinguishing red, green and white biscuit gun signals. Subjects with grade 2 scores will be able to distinguish red and green pyrotechnics if only those two colors are used. Subjects with grade 1 scores can distinguish red, green and yellow pyrotechnics.

INDICATIONS FOR FURTHER STUDY

In the previous sections it has been shown that in the selection and classification of air force personnel two types of color vision tests are needed. The basic screening test should provide a simple, rapid and reliable means of distinguishing normal from deficient color vision. The second test, to be given only to subjects who fail the basic test, should give a reliable and valid estimate of the degree of defect.

The abridged American Optical Company test appears at present to be the most suitable choice for the basic test. Consideration should, however, be given to the future development of some form of screening test in which there is no possibility that the applicant could memorize the correct answers. The S.A.M. anomaloscope might be a satisfactory substitute, although it is perhaps not so simple as chart tests. Unlearnable pseudoisochromatic charts might be constructed for example by using Landolt rings, the orientation of which could be changed. This principle has been employed in the Schaff test, published in France. A uniform pattern for the background in all charts as used in the new Navy test might be sufficient to prevent memorization.

Of the various quantitative tests investigated, the Color Threshold Test appears to be the most satisfactory for the classification of flying personnel, since the scores give a fairly reliable indication of ability to identify colored light signals. Data on the scores of a large group of subjects with deficient color vision not previously selected as to degree of defect would be of value in interpreting these scores on a percentile basis. Studies are also needed to provide further information as to the degree of defect in color vision compatible with the various duties of air force personnel.

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OPHTHALMIC PENICILLIN OINTMENTS

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FAVORABLE reports have been made on the treatment of certain surface infections of the border of the lid, the conjunctiva and the cornea with penicillin ointments. Florey and Florey [1] used a penicillin salve with a pure petrolatum base. Keyes [2] applied penicillin in a wool fat and cold cream base, and Cashell [3] in a lanette wax base.[4] In an earlier experimental investigation in this laboratory [5] the penetrability of three ointments, representing two types of emulsion systems (anhydrous wool fat containing 10 per cent liquid petrolatum and an oil-in-water emulsion) was studied; similar investigations were conducted by Bellows [6] with four bases and by Leopold and LaMotte [7] with a Carbowax (a polyethylene glycol) base. The cited experimental studies were, however, concerned mostly with the penetration from a few ointments, generally containing the sodium salt of penicillin. It was desirable, therefore, to extend the investigations and to compare the advantages of several ointment bases and penicillin compounds.

In the present study three properties of penicillin ointments were collated experimentally: first, their irritative action on the normal

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1. Florey, M. E., and Florey, H. W.: General and Local Administration of Penicillin, Lancet **1**:387 (March 27) 1943.

2. Keyes, J.: Penicillin in Ophthalmology, J. A. M. A. **126**:610 (Nov. 4) 1944.

3. Cashell, G. T. W.: Penicillin in Ocular Infections, Brit. M. J. **1**:420 (March 25) 1944.

4. For a description of the lanette wax base, see the composition of base 6 in the section on "Technic."

5. von Sallmann, L., and Meyer, K.: Penetration of Penicillin into the Eye, Arch. Ophth. **31**:1 (Jan.) 1944.

6. Bellows, J. G.: Penicillin Therapy in Ocular Infections, Am. J. Ophth. **27**:1206 (Nov.) 1944.

7. Leopold, I. H., and LaMotte, W. O., Jr.: Penetration of Penicillin in Rabbit Eyes with Normal, Inflamed and Abraded Corneas, Arch. Ophth. **33**:43 (Jan.) 1945.

rabbit and human eye; second, the stability of penicillin in various bases at room and at refrigerator temperature, and, third, the penetration of penicillin from the ointment into the eye. This subdivision is applied to the description of the experimental technic, as well as to the arrangement of the results. The problem of individual hypersensitivity to the mold product or to the ointment base was not dealt with, as it is of clinical nature; for the same reason, the first section on irritation was treated without reference to pathologic conditions of the eye.

TECHNIC

The investigations were limited to the sodium, calcium and ammonium salts of penicillin and to its free acid. With the exception of three salves supplied by pharmaceutical companies, the ointments were carefully made up in the pharmacy of the Presbyterian Hospital with a diversity of bases. When the sodium salt was used, it was dissolved in an appropriate dilution of the unitage given on the vial. The activity of the calcium and ammonium[8] salts was titrated by bioassay and expressed in Oxford units per milligram of the material. Weighed quantities were dissolved in calculated amounts of sterile isotonic solution of sodium chloride or were suspended in liquid petrolatum U. S. P. to obtain ointments of the hydrous (1 per cent moisture) or the anhydrous type, containing 1,000 Oxford units of penicillin per gram. Five of the salves were prepared with a hydrous and four with an anhydrous base. After the incorporation of the aqueous solution or oily suspension into the base and thorough mixing of the ingredients, the ointments were dispensed in collapsible tubes. One set was stored in the refrigerator at 32 F. and the other at a room temperature of 70 to 85 F. The preparations were tested within a week after they had been made, and the tests were repeated at intervals of four to sixteen weeks.

The sodium, ammonium and calcium salts of penicillin were incorporated in four to six, and the free acid in one, of the following bases:

1. Wool fat–petrolatum base, hydrous

	Gm.
Liquid petrolatum U. S. P.	10
Wool fat U. S. P.	50
White petrolatum	40

2. Wool fat–petrolatum base, anhydrous

3. S base, anhydrous

	Gm.
Light liquid petrolatum U. S. P. (Kaydol)	14
Wool fat U. S. P.	10
Petrolatum (grade Protopet no. 1)	36

4. Wool fat–cold cream base

	Gm.
Wool fat U. S. P.	25
Cold cream	75

Cold Cream

Spermaceti (cetyl palmitate)	6 Gm.
White wax	12 Gm.
Liquid petrolatum	50 Gm.
Sodium borate	1 Gm.
Distilled water	20 cc.

5. Hydrosorb—oleic acid ester, amide of diethanolamine, oleic acid and white petrolatum

6. Lanette wax base

8. Dr. Karl Meyer, of the department of ophthalmology, Columbia University College of Physicians and Surgeons, suggested the use of the ammonium salt of penicillin.

	Gm.
N-octadecyl alcohol	45
Sodium lauryl sulfonate	10
Cetyl alcohol	45
White petrolatum	50
Liquid petrolatum	75
Water	75

7. Vegetable oil base, hydrous. This base consists of hydrogenated peanut, soy bean and cottonseed oils.

8. Vegetable oil base, anhydrous.

9. L base, anhydrous. This base consists of Amerchol and petrolatum. Amerchol represents the nonsaponifiable residue of wool fat and is a mixture of sterols and sterol esters.

The irritative action on the conjunctival sac of normal rabbits after application of the ointments for two hours was judged by the presence and amount of hyperemia and secretion of the conjunctiva and occasionally by a slight haziness of the cornea. From parallel observations on the action of ointments containing the same salt but in different bases, it was possible to determine which component was responsible for the irritation. The tolerance of the human eye to the respective salves was determined by the same criteria and by the presence of symptoms of discomfort in 5 volunteers.

The stability of the penicillin in the ointment was evaluated after extraction from accurately weighed amounts of the ointment.[9] The samples were transferred to a separatory funnel, which contained 50 cc. of chloroform and 25 cc. of phosphate buffer (0.15 molar primary and 0.15 molar secondary phosphate in a proportion of 6:4). After the mixture had been shaken for five minutes and the fluids had settled, the chloroform was drained off and washed again with 25 cc. of the buffer solution. The extracts were combined in a centrifuge bottle, and remnants of the chloroform were thrown down by centrifugation for five minutes. In all steps of the procedure care was taken to keep the temperature low; the samples were placed on ice, the centrifuge bottles remained in the refrigerator and in one series they were spun in a low temperature centrifuge. Proportions of ointment and buffer solution were calculated to render a dilution of the incorporated penicillin to 10 Oxford units per cubic centimeter. Further dilutions of this solution were made, and the average of triplicate readings, obtained with the Oxford cup method, was computed against the standard curve for the day. It was calculated that approximately 15 per cent of the penicillin activity was lost during the procedure of extraction; but, since the initial penicillin content was taken as the amount of penicillin determined after the first extraction and therefore included this loss, as did subsequent determinations, it was not necessary to subtract it from each figure.

The penetration of penicillin from the ointments into the eye was studied on rabbits. For this purpose, the ointments were placed in the conjunctival sac, and aqueous fluid was withdrawn two hours later to estimate its antibacterial activity. For standardizing the technic, the following experimental conditions were observed: Light ether anesthesia was administered and was supported by the instillation and subcutaneous injection of 0.1 per cent nupercaine hydrochloride at the lid border prior to the insertion of two mattress sutures at corresponding positions in the margins of the upper and lower lids. While the lids were retracted, the ointment was squeezed from the tube and placed at the limbus in a way that a ribbon of the ointment circled twice the circumference of the cornea. Then the lids were closed by tying the sutures. After two hours the sutures and excess ointment were removed. Local anesthesia was again induced with nupercaine for withdrawal of aqueous, or the rabbits were killed for the

9. Dr. Karl Meyer furnished the technic of extraction and made other helpful suggestions.

excision of the cornea and conjunctiva. Usually 0.2 cc. of undiluted aqueous was used to ascertain the penicillin content with the Oxford cup method in four to six experiments for each ointment. In one series, in which the cornea and conjunctiva were tested for the presence of penicillin, extracts of these tissues were obtained in buffer solutions by grinding them with quartz sand.[5]

RESULTS

Irritation.—In general, the ointment bases and penicillin compounds which were examined were well tolerated by the normal rabbit and human eye. A transient stinging and burning sensation which was noted occasionally was considered negligible. It was more intense, however, with salves made with the Hydrosorb base. With this base, hyperemia, and in some instances a moderate degree of chemosis and a fine haze, of the cornea were noticed. The ammonium salt made up in the hydrous vegetable oil base (7) caused slight soreness, lasting for several hours, whereas the same salt in other bases was not irritating. None of the ointments gave rise to a conspicuous lesion of the corneal epithelium, such as Bellows described after the application of a vanishing cream. The rancid smell of the ointment containing the calcium salt in the anhydrous vegetable oil base (8) would make the preparation unsuitable for practical use.

Stability.—To our knowledge, there are no reports in which the decrease in activity of penicillin in ophthalmic ointments was determined with quantitative methods. The occasionally applied examination of the potency of the preparation by placing samples on seeded plates and observing the zones of inhibition is too crude to permit reliable conclusions. The decline in the activity of penicillin after various intervals of time is presented in table 1. The inactivation is expressed in per cent of loss from the initial penicillin activity as determined in the first week after the compounding of the ointment. The importance of the temperature of storage is evident in all instances except that of the ointment containing the calcium salt in the L base (9). In this ointment the salve retained 71 per cent of its initial activity after storage for twelve weeks at room temperature; another base containing the ammonium salt in the S base (3) retained 24 per cent of its initial activity at the same interval. The gradient of decline varied in the other preparations, but in most samples only traces [10] of penicillin activity were evident at the four or eight week interval.

When the ointments were stored in the refrigerator, the decrease in activity was much less but varied considerably with the salt and the base. With the sodium salt a minimal loss in the potency of the ointment was estimated for the hydrous vegetable oil base (7). Only 26 per cent of its initial penicillin activity was lost after storage for sixteen weeks, whereas with the anhydrous vegetable oil base (8), the

10. The term "trace" is applied here to the inhibition of growth within the cup in the Oxford method of penicillin determination.

hydrous wool fat–petrolatum base (1) and the wool fat–cold cream base (4)[11] the losses ranged between 40 and 50 per cent after twelve weeks' storage. The ointments containing the ammonium salts also retained their activity well when prepared in the hydrous vegetable oil base (7). After twelve weeks no inactivation was noticed. The S base (3) and the anhydrous vegetable oil base (8) were less stable, with a loss of 31 to 44 per cent in their penicillin activity at the end of the same period.

The ointments with the calcium salt showed an optimum of stability as manufactured in the L base (9). In this preparation no appreciable

TABLE 1.—*Loss of Penicillin Activity in Ointments at Refrigerator and Room Temperatures*

Penicillin Compound	Ointment Base	Type of Storage	Per Cent Loss of Initial Penicillin Activity After			
			4 Wk.	8 Wk.	12 Wk.	16 Wk.
Sodium Salt	Wool fat-petrolatum, hydrous	Refrigerator	..	36	43	49
		Room temperature	..	49	72	T
	Wool fat-petrolatum, anhydrous	Refrigerator	..	71.9	T	..
		Room temperature	..	T	..	..
	Wool fat-cold cream	Refrigerator	20	24	44	..
		Room temperature	63	..	T	..
	Vegetable oil base, hydrous	Refrigerator	No loss	7	10	26
		Room temperature	14	T	..	..
	Vegetable oil base, anhydrous	Refrigerator	..	18	43	..
		Room temperature	..	T	..	..
Ammonium Salt	Vegetable oil base, hydrous	Refrigerator	No loss	No loss	No loss	32
		Room temperature	T	..	..	..
	Vegetable oil base, anhydrous	Refrigerator	..	15	31	..
		Room temperature	T	..	..	..
	S base	Refrigerator	5	18	44	..
		Room temperature	12	40	76	..
Calcium Salt	Vegetable oil base, hydrous	Refrigerator	56	..	67	..
		Room temperature	T	..	..	..
	Vegetable oil base, anhydrous	Refrigerator	8	..	30	..
		Room temperature	T	..	..	..
	S base	Refrigerator	18	..	43	..
		Room temperature	T	..	..	..
	L base	Refrigerator	..	No loss	No loss	..
		Room temperature	..	No loss	29	..
Free Acid	S base	Refrigerator	4	9	15	..
		Room temperature	35	53	T	..

T = reduced to a trace of penicillin activity.

decrease in activity was noticed at refrigerator temperature twelve weeks after the first determination. The hydrous vegetable oil base (7) lost 67 per cent; the anhydrous vegetable oil base (8) lost 30 per cent and the S base (3) lost 43 per cent, of the initial penicillin potency at the same interval.

The free acid was supplied only in one base (3). At refrigerator temperature the decrease in activity was moderate; that is, it lost 15 per cent after twelve weeks.

11. Tentative experiments revealed that spermaceti, a constituent of the wool fat–cold cream base, inhibited the activity of penicillin. A 1 per cent solution of this ingredient caused a 50 per cent loss in the potency of a penicillin solution containing 10 Oxford units per cubic centimeter.

Experiments with ointments containing the sodium salt in a lanette wax base (6) were discontinued because the separation of the aqueous phase in the emulsion system resulted in great variations in the penicillin content of gravimetrically indentical samples of the ointment.

In conclusion the experiments on the stability of four penicillin compounds in various ointment bases showed the superiority of two types of ointments: the hydrous vegetable base with the sodium and ammonium salts and the L base, which was supplied with the calcium salt. The latter was the only preparation which retained much of its original potency after storage for twelve weeks at room temperature. These investigations on the stability of ophthalmic ointments disclosed no specific advantage in the use of any particular salt of penicillin or its free acid.

Determinations were not continued over a longer period of storage because, with the intensive investigations of the many commercial research laboratories in the manufacture of ophthalmic penicillin ointments, it is likely that such a product which is stable at unfavorable temperatures will be available in the near future. In view of this, greater emphasis was placed on the experiments relating to the resorption of penicillin from the various ointment bases into the eye.

Penetration.—The penetration of penicillin into the cornea and the conjunctiva was investigated in a series of 12 eyes. It was technically impossible to remove completely the excess ointment from the surface of the tissues without changing the content of penicillin in the specimens. This and other inaccuracies in handling and extracting the ground tissue led to such erratic results that further measurements were not attempted. Readings on the antibacterial activity of the aspirated aqueous were more consistent and are shown in table 2.

When ointments with the sodium salt of penicillin were used, the highest average concentration of penicillin in the aqueous (0.6 Oxford unit per cubic centimeter) was determined by the resorption from the lanette wax base (6), but the values were very low in 2 instances. The discrepancy in the results can be explained by the instability of the ointment base, as described in the previous section. The penetration from the hydrous vegetable oil base (7) was satisfactory, with an average of 0.51 Oxford unit per cubic centimeter of aqueous. Resorption from the wool fat–cold cream base (4) was about one-half that from the hydrous vegetable oil base. Only traces of penicillin activity were estimated, however, with the wool fat–petrolatum bases (1 and 2) and with the vegetable oil base prepared with an anhydrous base (8).

In contrast to the poor penetration of sodium penicillin in the anhydrous wool fat–petrolatum base (2) was that of the ammonium salt in a similar base (3). Here relatively high readings were recorded with 0.61 Oxford unit per cubic centimeter of aqueous. The

concentration of 0.53 Oxford unit, determined after the use of the ammonium salt in the hydrous vegetable oil base (*7*), was similar to that after the application of the sodium salt in the same base. The

TABLE 2.—*Penetration of Penicillin into the Aqueous Two Hours After Placing Ointment in Conjunctival Sac*

Penicillin Compound	Ointment Base	Oxford Units Penicillin per cc. Aqueous
Sodium Salt	Wool fat-petrolatum, hydrous	Traces *
	Wool fat-petrolatum, hydrous	Traces
	Wool fat-cold cream	0.18
		0.46
		0.23
		Trace
	Average	0.23
	Lanette wax	0.24
		0.69
		1.43
		Trace
	Average	0.6
	Vegetable oil base, hydrous	0.44
		0.32
		0.63
		0.63
	Average	0.51
	Vegetable oil base, anhydrous	Traces
Ammonium Salt	S base	1.0
		0.83
		0.64
		0.48
		0.56
		0.17
	Average	0.61
	Vegetable oil base, hydrous	0.89
		0.1
		1.0
		0.79
		0.2
		0.15
	Average	0.53
	Vegetable oil base, anhydrous	0.19
		0.15
		1.38
		Trace
		Trace
		Trace
	Average	0.29
Calcium Salt	S base	Traces
	Vegetable oil base, hydrous	0.99
		0.41
		0.41
		1.75
	Average	0.89
	Vegetable oil base, anhydrous	0.15
		Trace
		0.27
		Trace
	Average	0.13
	L base	0.6
		0.53
		1.22
		0.8
	Average	0.79
Free Acid	S base	Traces

* Trace indicates 0.05 Oxford unit.

penicillin content of the aqueous after the use of the ointment with the anhydrous vegetable oil base (8) was about one-half that obtained with the hydrous type of this base.

The best penetration from ointments containing the calcium salt was ascertained with the hydrous vegetable oil base (0.89 Oxford unit per cubic centimeter of aqueous). Slightly lower (0.79 Oxford unit per cubic centimeter of aqueous) was that from the L base 9), whereas the resorption from the anhydrous vegetable oil base (8) and from the S base (3) was very little. Equally unsatisfactory was the resorption from the latter base containing the free acid (0.08 Oxford unit per cubic centimeter). In general, the penetration of penicillin into the eye was highest from ointments containing the calcium salt, less from ointments with the sodium and ammonium salts and lowest from the one ointment with the free acid.

Because of the differences in the technics it is scarcely possible to compare the results of this study with previous investigations on the penetration of penicillin from ointments into the eye. In earlier experiments reported by this laboratory the ointments which were used contained penicillin of very low potency and the aqueous did not exhibit any antibacterial activity. Leopold and LaMotte,[7] using an ointment containing 500 Oxford units of sodium penicillin per gram of Carbowax base (polyethylene glycol), also did not detect any inhibitory action of the aqueous in normal rabbit eyes. Bellows'[6] experiments disclosed a concentration of 0.42 Oxford unit of penicillin per cubic centimeter of aqueous with a wool fat ointment and 0.38 Oxford unit per cubic centimeter with an oil-in-water emulsion. Both ointments contained 2,500 Oxford units of sodium penicillin per gram of base and were not irritating.

The composition of the wool fat–petrolatum base (1) used in the present study was similar to that applied by Bellows but gave the lowest values for penicillin in the aqueous, as only traces could be determined. The penicillin content of this ointment declined to about one half of its original potency after sixteen weeks' storage in the refrigerator. Despite the lower unitage in our preparations, the penicillin concentration of the aqueous after the application of several ointments ranged slightly higher than that reported by Bellows. Significantly greater, however, were the figures obtained after the application of the stable salve containing the calcium salt in the L base (9).

In conclusion, of the many penicillin ointments tested, the requirements for a nonirritating, relatively stable and well penetrating preparation for ophthalmic use were best fulfilled by the following bases: the hydrous vegetable oil base (7), with the sodium salt, and the L base (9), supplied only with the calcium salt.

SUMMARY

1. Of the series of nine ointment bases which were tested, two were irritating to the eye. No irritation could be attributed to any of the four penicillin compounds which were incorporated in the ophthalmic ointments.

2. The potency of the penicillin in the salves was relatively stable in one hydrous and two anhydrous bases after twelve to sixteen weeks in the refrigerator. Storage at room temperature resulted usually in a rapid loss of potency except for two ointments prepared with an anhydrous base. No difference in the stability of the various ointments could be ascribed to the penicillin compound in the salves.

3. The penetration of penicillin into the aqueous of rabbits was substantial from one hydrous and two anhydrous bases. After the application of two ointments with the calcium salt, the content of penicillin in the aqueous exceeded that after the use of salves with the sodium and ammonium salts. The resorption of penicillin was unsatisfactory from the one ointment which contained the free acid of penicillin.

The Schering Corporation supplied the ammonium salt of pencillin and the ointments containing the free acid and the ammonium salt in the S base, and the Lederle Laboratories, Inc., the ointment containing the calcium salt of penicillin in the L base.

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EFFECTS OF ATROPINE SULFATE, METHYLATROPINE NITRATE (METROPINE) AND HOMATROPINE HYDROBROMIDE ON ADULT HUMAN EYES

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CERTAIN details of the clinical actions of several mydriatics of the belladonna group are given in tables in the textbooks of pharmacology of Sollmann [1] and Goodman and Gilman,[2] but the relative speeds and durations of the actions of the various drugs are not well defined because (*a*) the solutions used varied in strength from 0.5 to 10 per cent and (*b*) doses are not given. It appeared desirable, therefore, to gather data permitting a more exact comparison of the actions of some of these drugs. Atropine seemed the logical choice as the standard with which homatropine and methylatropine nitrate (Metropine) should be compared.

Of the many authors who have described the mydriatic and cycloplegic effects of atropine, homatropine and methylatropine nitrate, only a few have given data pertinent to the present investigations. Consideration of dosage being omitted for the moment, the time for maximal effect and the approximate time of recovery may be briefly described. Atropine produces maximal mydriasis in about thirty to forty minutes, with complete recovery in twelve days, and maximal cycloplegia in a few hours, with recovery in a few days to perhaps as long as eighteen days (Marron [3]). Homatropine produces maximal mydriasis in seven to thirty minutes, with recovery in six to ninety-six hours, and maximal cycloplegia in thirty to ninety minutes, with recovery in ten to forty-eight hours (Bertheau,[4] Jackson,[5] Marron,[3] Risley,[6] Schell [7] and Tweedy and Ringer [8]).

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This work was supported in part by a grant from the R. J. Strasenburgh Company, Rochester, N. Y.

1. Sollmann, T.: A Manual of Pharmacology and Its Application in Therapeutics and Toxicology, Philadelphia, W. B. Saunders Company, 1942.

2. Goodman, L., and Gilman, A.: Pharmacological Basis of Therapeutics, New York, The Macmillan Company, 1941.

3. Marron, J.: Cycloplegia and Mydriasis by Use of Atropine, Scopolamine and Homatropine-Paredrine, Arch. Ophth. **23**:340 (Feb.) 1940.

(Footnotes continued on next page)

Methylatropine nitrate produces approximate maximal mydriasis in thirty to seventy-five minutes, with recovery in forty to seventy-two hours, and maximal cycloplegia in two to fourteen hours, with recovery in thirty-six hours (Goldberg,[9] Lindenmeyer[10]). These data illustrate the general opinion that atropine is much more lasting in its effects on the eye than is homatropine or methylatropine nitrate.

We were interested in comparing the mydriatic and cycloplegic effects of these three drugs on human eyes that had received the same dose of each drug. Goldberg[9] had compared equal strengths of homatropine and methylatropine nitrate against solutions of atropine only one-tenth as concentrated. Blume[11] had used 1 per cent solutions of each of the three drugs in the eyes of cats. Our technic was to instil a single drop of a solution of 1 per cent atropine sulfate, 1 per cent methylatropine nitrate or 1 per cent homatropine hydrobromide. A series of 46 eyes were studied, the distribution according to the patients' ages being shown in the following tabulation.

Patient's Age, Yr.	Number of Eyes
16-20	8
21-25	22
26-30	12
31-37	4

Diameters of the pupils were generally measured with a V pupillometer under fairly uniform lighting conditions. With 6 eyes entoptic pupillometry (Cogan[12]) was employed. With the two methods pupillary diameters were reproducible within 0.5 mm. Amplitude of accommodation was measured by the difference of near and far point reciprocals. Six point newsprint on a slide on a meter stick was used to ascertain these points. When necessary, a lens sufficient to keep the far point between 0.66+ and 1 meter from the eyes was added to the system.

4. Bertheau, H.: Das Homatropin, Berl. klin. Wchnschr. **17**:581, 1880.

5. Jackson, E.: Homatropin Hydrobromate, M. News, Philadelphia **49**:88, 1886.

6. Risley, S. D.: The Value of Homatropine Hydrobromate in Ophthalmic Practice, Am. J. M. Sc. **81**:113, 1881.

7. Schell, H. S.: A New Mydriatic, Philadelphia M. Times **11**:7, 1880.

8. Tweedy, J., and Ringer, S.: Mydriatic Properties of Homatropin, or Oxytoluyltropein: Its General Physiological Action, Lancet **1**:795, 1880.

9. Goldberg, H.: Versuche mit Eumydrin, einem Ersatzmittel des Atropinsulfates, Heilkunde **7**:97, 1903.

10. Lindenmeyer, O.: Eumydrin, ein neues Mydriaticum, Berl. klin. Wchnschr. **40**:1072, 1903.

11. Blume, W.: Ueber eine die Pupille verengende Wirkung des Atropins, Arch. f. exper. Path. u. Pharmakol. **164**:226, 1932.

12. Cogan, D. G.: A Simplified Entoptic Pupillometer, Am. J. Ophth. **24**:1431, 1941.

The solutions were adminstered according to the plan shown herewith. Each subject in the study received one drug in his right eye and the same or another drug in his left eye.

No. of Pairs of Eyes	Right Eye	Left Eye
11	Atropine sulfate	Methylatropine nitrate
2	Atropine sulfate	Atropine sulfate
7	Homatropine hydrobromide	Methylatropine nitrate
2	Methylatropine nitrate	Methylatropine nitrate
1	Control	Methylatropine nitrate

The anisopia bothered some of the subjects considerably and made walking and grasping objects somewhat uncertain. For example figure 1 illustrates the different amounts of mydriasis obtained in a subject who received atropine in his right eye and methylatropine in his left eye.

Figures 2, 3 and 4 show the data for changes in time of accommodation and in size of pupils. During the first hour represented by each curve, readings were made at short intervals (abscissas, in minutes);

Fig. 1.—Mydriasis produced in the right eye by 1 drop of 1 per cent solution of atropine sulfate and in the left eye by 1 drop of a 1 per cent solution of methylatropine nitrate.

additional readings were made at six hours and thereafter up to fourteen days for atropine and methylatropine and up to eleven days for homatropine. Although many eyes were followed for up to fourteen days, measurements were discontinued as the values for each subject approached the original normal values.

To allow the curves for mydriasis and cycloplegia to run parallel courses, the units of accommodation plotted were $100/D_t$, where D_t was the number of diopters of accommodation at any time, t. This allows somewhat more satisfactory inspection of the graphs. Various subjects have characteristic marks in these figures, so that the course of the effects on one person may be followed through the entire period. The general trends for each drug are similar, but variation in individual responses is clearly shown by the wide scatter of points above and below the trend lines which are indicated. In figure 5 the average curves are reproduced so that the comparative effects of atropine, homatropine and methylatropine are shown side by side.

Average Mydriatic and Cycloplegic Effects of Atropine, Methylatropine Nitrate and Homatropine

Drug	Number of Eyes	Initial Pupillary Diameter (P_o)	Time to Maximum		Maximum Pupillary Diameter (P_t)	Maximal Dilation Ratio (P_t/P_o)	Residual Accommodation (D_t/D_o)	Time to Onset of Recovery of		Fifth Day		
			Mydriasis	Cycloplegia				Mydriasis	Cycloplegia	Pupillary Diameter (P_t)	Dilation Ratio (P_t/P_o)	Residual Accommodation (D_t/D_o)
Atropine	16	3.4	40 min.	5 hr.	8.3	2.44	0.21	6 hr.	1 day	5.2	1.54	0.60
Methylatropine	23	3.3	50 min.	5 hr.	7.7	2.32	0.29	6 hr.	6 hr.	3.8	1.15	0.71
Homatropine	7	3.4	40 min.	25 min.	5.9	1.72	0.55	6 hr.	1 hr.	3.3	0.97	1.0

In the table are given the number of eyes treated with each drug, the times required for maximum mydriasis and maximum cycloplegia, the initial and maximum pupillary diameters, the maximum ratios of pupillary diameters, the minimum remaining fractions of accommodation, the times to onset of recovery from mydriasis and cycloplegia and the observations on diameter of the pupil and residual accommodation made on the fifth day.

The table shows that the times to maximum mydriasis were approximately the same for the three drugs but that times for recovery were in

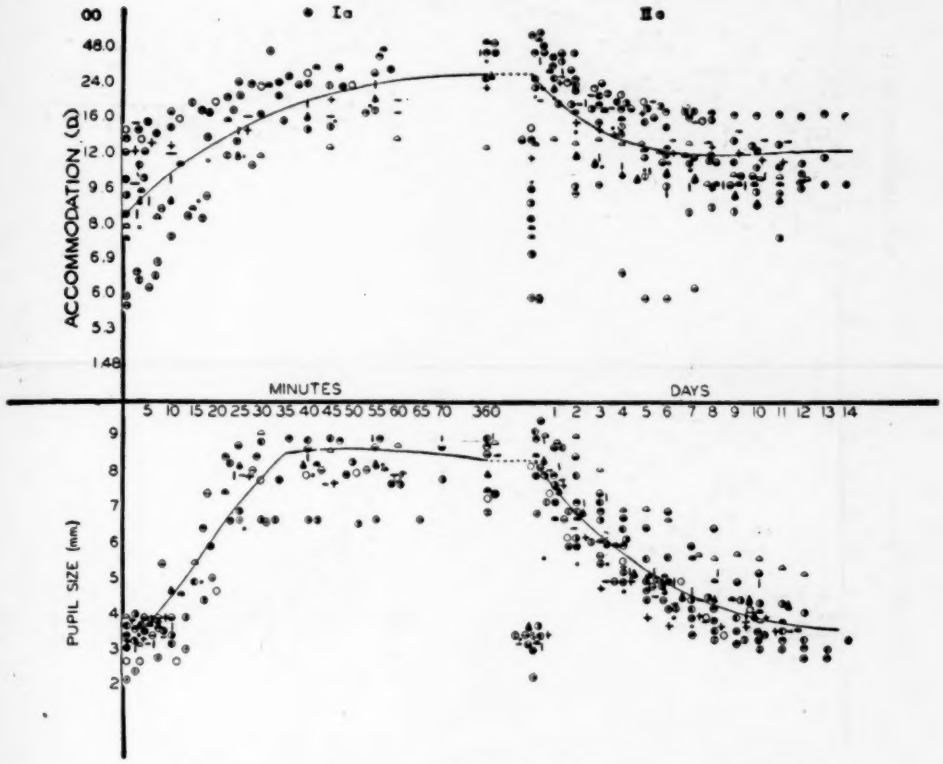

Fig. 2.—Changes in time of accommodation and of pupillary size after administration of 1 drop of 1 per cent solution of atropine sulfate. During the first hour readings were made at short intervals. Additional readings were made at six hours and thereafter, up to fourteen days. Accommodation is plotted as units $100/D_t$, where D_t is the number of diopters of accommodation at any time, t.

the following order: homatropine <methylatropine <atropine. Homatropine had a less dilating effect than either methylatropine or atropine.

Homatropine had a considerably more rapid action in producing maximum cycloplegia than did either methylatropine or atropine. Again, homatropine was less potent than the other two drugs, and methyl-

atropine had somewhat less effect than atropine. The recovery from the cycloplegic effects of homatropine was more rapid than that from the effects of methylatropine or atropine. Paralysis of accommodation from methylatropine began to disappear more quickly than that from atropine, but the speeds of recovery were not markedly different for the two drugs.

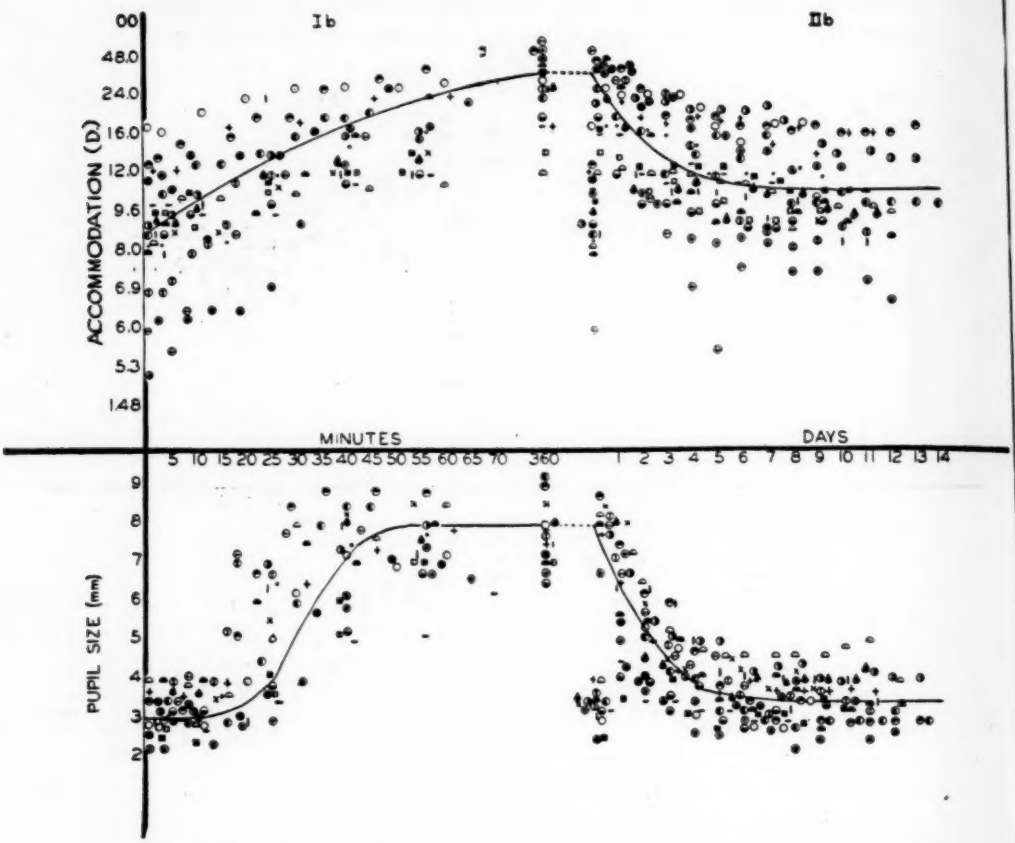

Fig. 3.—Changes in time of accommodation and pupillary size following the administration of 1 drop of 1 per cent of solution of methylatropine nitrate. See legend of figure 2.

COMMENT

This work demonstrates that the effects of atropine, methylatropine and homatropine on the size of the pupil and the accommodating ability of the eye are essentially similar; the chief difference is in the degree of activity. An inspection of figures 2, 3 and 4 shows that for each drug there was a wide variation in response of subjects.

The maximum diameters of the pupils of 8.3 and 7.7 mm. for atropine and methylatropine, respectively, are significantly different by the t test (Fisher[13]) (p is less than 0.01). Thus, it is seen that both homatropine and methylatropine had weaker actions in producing dilation of pupils than did atropine. The speeds with which the three drugs produced their maximum effects were roughly the same; and the speeds of recovery from the mydriatic effects of methylatropine and

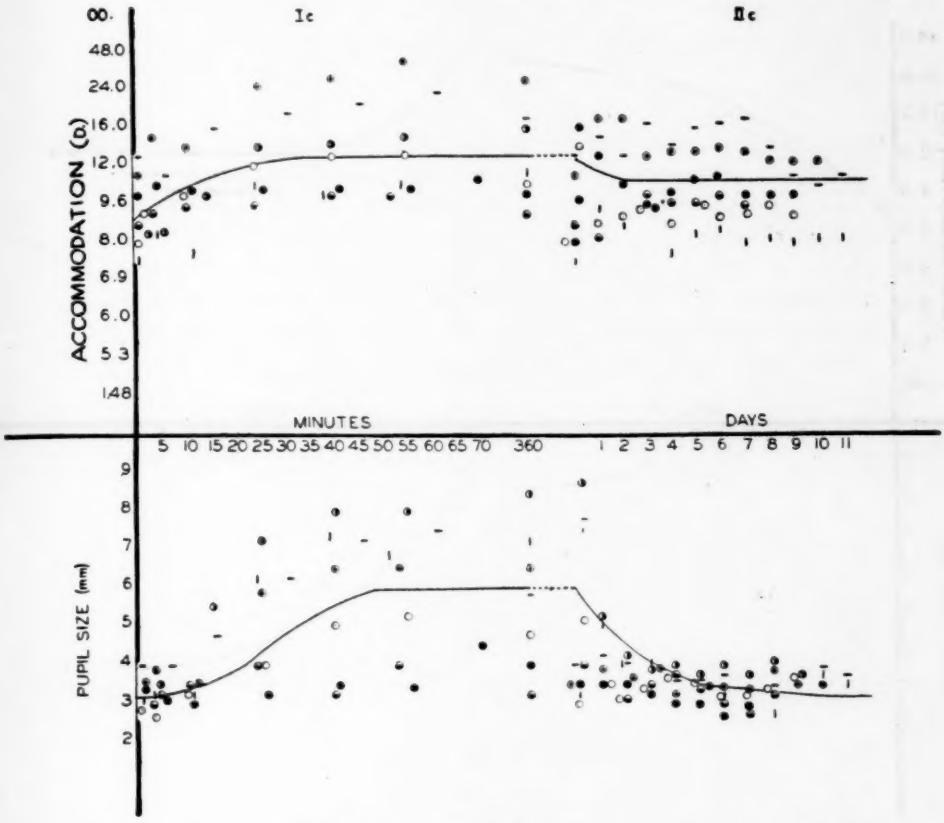

Fig. 4.—Changes in time of accommodation and of pupillary size following the administration of 1 drop of 1 per cent solution of homatropine hydrobromide. See legend of figure 2.

homatropine were significantly less than the speed of recovery from atropine.

The amount of cycloplegia produced by homatropine was significantly less than that produced by comparable doses of atropine or

13. Fisher, R. A.: Statistical Methods for Research Workers, ed. 9, London, Oliver & Boyd, Ltd., 1944.

methylatropine. The time required for maximum effect with homatropine was approximately one-twelfth that required by the other drugs. However, inspection of figure 5 shows that the three curves of loss of accommodation ran roughly parallel during the first few minutes after instillation of the drugs into the eyes. This would make it seem possible that the short time required for homatropine to produce its maximum effect, as compared with the time required for the other two drugs, may be correlated with the weakness of the action of homatro-

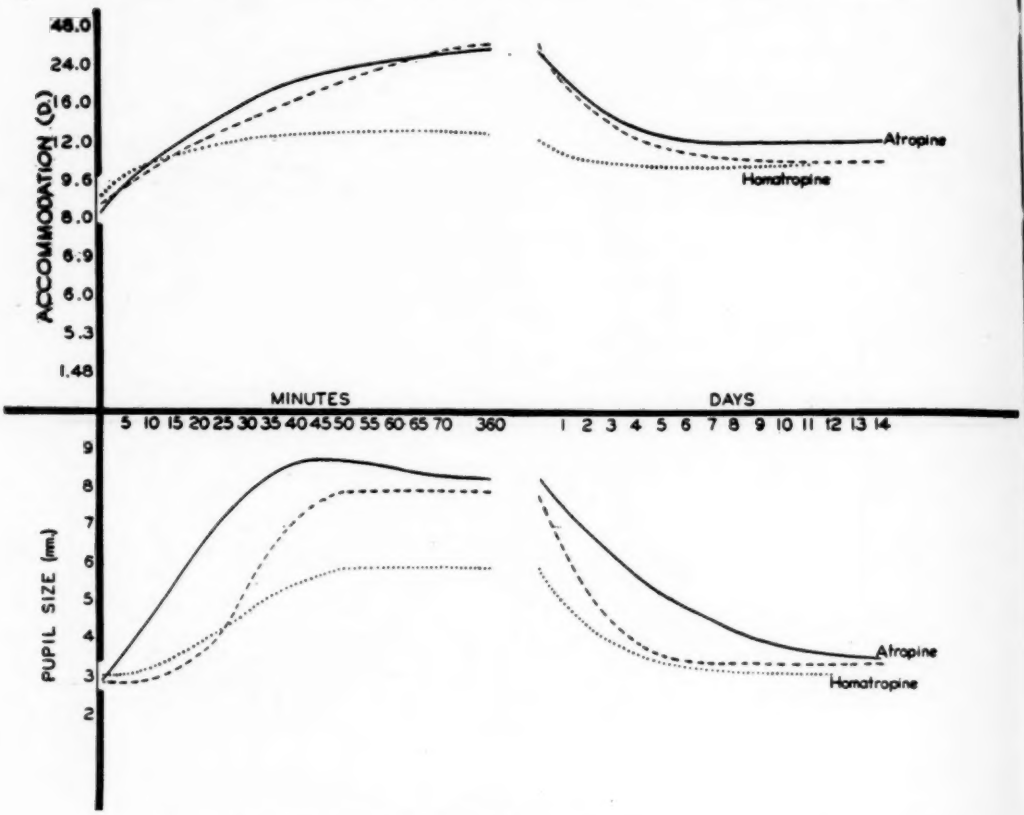

Fig. 5.—Average curves of changes in time of accommodation and of pupillary size following the administration of 1 drop of 1 per cent solutions of atropine sulfate, methylatropine nitrate and homatropine hydrobromide. See legend of figure 2.

pine. Similarly, the relatively more rapid recovery from the homatropine cycloplegia may also, in part at least, be explained by the weak effect of the drug.

While methylatropine produced approximately the same amount of paralysis of accommodation as the same dose of atropine, and in approximately the same time, the time for recovery from methylatropine

(6.8 ± 3.8 days) was possibly somewhat shorter than that for atropine (9.2 ± 3.6 days). The difference is not significant by the t test. The fact that methylatropine produced as much cycloplegia and almost as much mydriasis as atropine, and may have permitted somewhat earlier recovery of these two ocular functions, suggests that methylatropine might be a suitable substitute for atropine in ophthalmic practice. As suggested by Goldberg,[9] it might be particularly advantageous for use in children, in whom homatropine usually has an unsatisfactory action. It appears that methylatropine would permit about as easy refraction as atropine and might allow somewhat faster recovery of normal ocular functions.

SUMMARY

Atropine sulfate, methylatropine nitrate or homatropine hydrobromide was instilled in equal amounts into human eyes.

Under these conditions homatropine had less mydriatic and cycloplegic effect than either of the other two drugs, and recovery from its effects was the most rapid.

Methylatropine nitrate had significantly less mydriatic action than atropine. The cycloplegic action was about the same as that of atropine.

Dr. J. H. Wills, Jr., gave assistance in this study.

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NIGHT VISION

II. A Comparison and Critique of Various Procedures Used for Night Vision Testing

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IN A previous article [1] comparative data on the results of examination of night vision of 217 Caucasian and 217 Japanese students were reported. The purpose of the present paper is to furnish statistical data on the correlation that was found between the instruments used, to describe briefly some of the other instruments and technics employed in night vision testing and to proffer a plan, based on physiologic and optical principles, for universal adoption for the complete examination of the function of night vision.

COMPARISON OF FIVE INSTRUMENTS

The instruments used in the previous survey included the Hecht-Shlaer adaptometer, the S.A.M. Night Vision Tester, the Luckiesh-Moss Low Contrast Test Chart, the Harman Disc Spotting Device and the Ferree-Rand Projectochart. Of the results obtained with these instruments, the figures obtained on the Hecht-Shlaer adaptometer, for the examination of the light threshold, and the scores achieved on the S.A.M. Night Vision Tester were chosen for purposes of comparison with the data obtained with all the other devices.

The accompanying tables are statistical compilations of the responses obtained from the entire group (434 subjects) on all the instruments used during these examinations, appearing in contrast with the two arbitrarily selected standards. In both tables, the subjects were assigned superior, satisfactory or unsatisfactory ratings. The bases of these groupings appear at the head of each column in both tables. It should be noted that in tests with the Hecht-Shlaer adaptometer only those subjects were given superior scores whose light thresholds did not exceed 2.2 log units. This is a slight departure from previous methods of scoring and was done only for the purpose of obtaining a more accurate statistical analysis.

Inspection of the data compiled in tables 1 and 2 shows that though there is some correlation between the responses obtained on the various instruments this is by no means uniform and consistent. Yet the tests

1. Holmes, W. J.: Night Vision: I. Comparison of the Scotopic Visual Ratings of Young Japanese and Caucasian Adults Living in Hawaii, Arch. Ophth. **36**:141 (Aug.) 1946.

were carried out by the same examiner, using the same technic on subjects of the same age and of approximately the same level of intelligence. This would suggest that either the instruments were at fault or that dissimilar retinal functions were tested, which do not lend themselves to purposes of comparison. Apparently, both these assumptions are at least partially correct. To illustrate: On the Hecht-Shlaer adaptometer, 153 subjects were rated as superior on the basis

TABLE 1.—*Correlation of the Results of Examinations for Night Vision of 434 Subjects Obtained on the S.A.M. Night Vision Tester with Scores in Other Tests*

	Scores on S.A.M. Night Vision Tester			
	Superior (8 and 9)	Satisfactory (5 to 7)	Unsatisfactory (0 to 4)	Total
No. of Subjects	50	310	74	434
Hecht-Shlaer adaptometer				
Light thresholds (log units)				
1.5 to 2.9	50	249	51	350
3.0 to 3.9	..	50	22	772
4.0 and above	..	11	1	12
Form thresholds (log units)				
2.5 to 3.9	47	240	38	334
4.0 to 4.9	3	50	24	77
5.0 and above	..	11	12	23
Disc Spotting Test (Harman)				
At distances of 10′ to 9′	40	140	16	196
8′ to 7′	4	85	28	117
6′ to 5′	5	71	23	90
4′ or less	1	14	7	22
Ferree-Rand Projectochart equipped with neutral filter and with				
Shutter fully closed	41	147	13	201
Shutter open to 0.25	6	141	50	197
Shutter open to 0.33	3	13	10	26
Shutter open to 0.50	..	9	1	10
Shutter open to 0.75	..	..	..	..
Luckiesh-Moss Low Contrast Test Chart				
At 10′, read lines 20 and 19	12	35	5	52
At 10′, read lines 18 and 17	8	50	4	62
At 10′, read lines 16 and 15	4	28	2	34
At 10′, read lines 14 or less	15	26	3	44
At 9′, read line 20	4	45	7	56
At 8′, read line 20	1	48	15	64
At 7′, read line 20	3	28	15	46
At 6′, read line 20	2	28	8	38
At 5′, or less read line 20	1	22	15	38

of their low light threshold levels; on the S.A.M. Night Vision Tester only 50 subjects were given superior scores. Thus, on a cursory examination it would seem that there is little, if any, correlation between the results obtained with the two procedures. However, on closer scrutiny one finds that in one test the measurements involved the light threshold and in the other the form threshold. In one procedure the time element was a known, standard factor, while in the other it changed with every click of the shutter.

OTHER TESTING TECHNICS

As a further illustration, in order to emphasize that dissimilar technics may be responsible for incongruous results, a brief description

of various instruments frequently mentioned in the literature is given as follows:

Device 9-B-4, a radium plaque adaptometer, is used for the determination of the form threshold at a distance of 5 feet (1.5 meters). The background is a luminous radium plaque, on which the test object, consisting of the letter T, may be rotated in four different meridians.

TABLE 2.—*Correlation of the Results of Examination for Night Vision of 434 Subjects by Five Different Methods and Comparison with Measurements of Their Light Thresholds as Expressed on the Hecht-Shlaer Adaptometer*

	Light Threshold (log units) Obtained on Hecht-Shlaer Aadaptometer			
	Superior (1.5 to 2.2)	Satisfactory (2.3 to 2.9)	Unsatisfactory (3.0 and Above)	Total
No. of Subjects	153	224	57	434
S.A.M. Night Vision Tester				
Lightest filter 0 to 4	6	74	23	103
5	12	52	21	85
6	48	28	10	86
7	56	20	3	79
8	27	41	..	68
Darkest filter 9	4	9	..	13
Hecht-Shlaer adaptometer form threshold (log units)				
2.5 to 3.9	143	124	14	281
4.0 to 4.9	8	77	25	110
5.0 and over	2	23	18	43
Disc Spotting Test (Harman)				
At distances of 10′ to 9′	92	93	11	196
8′ to 7′	43	61	13	117
6′ to 5′	9	60	30	99
4′ or less	9	10	3	22
Ferree-Rand Projectochart equipped with neutral filter with				
Shutter fully closed	97	95	9	201
and				
Shutter open to 0.25	43	114	40	197
Shutter open to 0.33	11	10	5	26
Shutter open to 0.50	2	5	3	10
Shutter open to 0.75	..	..	..	..
Luckiesh-Moss Low Contrast Chart				
At 10′, read lines 20 and 19	28	19	5	52
At 10′, read lines 18 and 17	31	28	3	62
At 10′, read lines 16 and 15	20	13	1	34
At 10′, read lines 14 or less	32	11	1	44
At 9′, read line 20	14	38	4	56
At 8′, read line 20	9	48	7	64
At 7′, read line 20	4	29	13	46
At 6′, read line 20	6	20	12	38
At 5′, or less read line 20	9	18	11	38

The A.A.F. Eastman Night Vision Tester likewise measures the form threshold. The test object is a 1 degree Landolt C. The highest level of intensity for the apparatus is 6.25 micromicrolamberts.

An adaptometer described by Riddell [2] consists in a modification of the Birch-Hirshfeld instrument and is so designed that a relatively constant portion of the retina is tested in an area where there is an approximately equal distribution of rods and cones.

2. Riddell, W. J. B.: On Testing Dark Adaptation, Glasgow M. J. **139**:149-157 (June) 1943.

The Koch adaptometer [3] is a modification of the Hecht instrument. The light source in this apparatus is a 25 watt bulb. The light is passed through several filters and graduated to a range of 2 to 6 micromillilamberts by two variables, the diaphragmatic aperture and the speed of a compur shutter. There are fixation points, consisting of radium salt, for either eye so placed that the light falls on the retina 6 degrees from the fovea. For testing form sense a 10 mm. rotating E is used, which is placed 380 mm. from the patient's eyes. Each eye is tested separately.

Solandt and Best,[4] in Canada, have used another modification of the Hecht-Shlaer apparatus. They reported variations on successive examinations which range from 0.06 to 0.17 log units and concluded that the instrument in their hands has been of value in furnishing consistent results.

Yudkin, Robertson and Yudkin [5] used an instrument modified from the Crookes adaptometer. Their technic consists in adapting the subject to light and then measuring the retinal thresholds repeatedly over a period of forty minutes. They stressed the importance of evaluating dark adaptation in terms of entire function, that is, the cone threshold, the rod threshold, the transition time between the two phases and the final rod threshold level. They expressed the belief that adaptometers which measure the visual threshold only at one particular time are misleading and in many cases erroneous.

An instrument which has gained wide acceptance in the British army is the rotating pentagon.[6] The test object in this apparatus is a large V mounted in five different positions on a translucent screen, illuminated by a small bulb run from a dry battery and controlled by a rheostat and a voltmeter. The lamp is situated at varying distances from each of the five screens. The test is performed in a darkened hut, with the subject seated at a distance of 1 meter from the instrument.

A test has been devised by Metcalfe [7] based on the fact that after exposure to glare preception of green is the last color to return to normal.

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3. Michaelson, I. C.: Defective Night Vision Among Soldiers: Dark Adaptation Results and Their Use in Diagnosis, Brit. J. Ophth. **28**:140-147 (March) 1944.

4. Solandt, D. Y., and Best, C. H.: Night Vision, Canad. M. A. J. **49**:17-21 (July) 1943.

5. Yudkin, J.; Robertson, G. W., and Yudkin, S.: Vitamin A and Dark Adaptation, Lancet **2**:10-13 (July) 1943.

6. Rycroft, B. W.: Night Vision in the Army, Brit. M. J. **2**:576-577 (Nov. 14) 1942.

7. Metcalfe, E. E.: A New Method for Determining Night Blindness: Preliminary Report, U. S. Nav. M. Bull. **38**:231-239 (April) 1940.

Much has been written about the biophotometer. As recently as May 1944, Schonberg [8] stated that he found the biophotometer invaluable in cases in which vitamin A deficiency has been suspected and as an aid in diagnosis of those conditions in which night blindness is one of the symptoms. However, Oldham and his associates [9] reported that the relationship between the readings in the biophotometer test and the nutritional status with respect to vitamin A was not close enough to warrant the continued use of this test as a means of diagnosing subclinical vitamin A deficiencies.

Saubermann [10] studied the power of discriminating differences in luminosity by means of an apparatus on which colored disks can be rotated. In an outer circular portion a colored ring is exposed for comparison with brightness of an inner circular disk, in which the relative quantities of white and black can be changed, using rotation. Differences in luminosity are reported to be less easily perceived as dark adaptation increases.

An instrument called the umbralometer has been described by Costi Garcia de Tunon.[11] This apparatus consists of a 4 volt lamp, a battery with variable resistance, a collimator and a pair of Nicol prisms. By rotation, the Nicol prisms serve as means of obscuration; the zero point is reached when there is complete crossing of the prisms. The advantages claimed for this device are the continuous control of the intensity of the current and of the mechanism of obscuration, elimination of the factor of accommodation, the possibility of making observations in the presence of low visual acuity and the basing of the measurements not on light perception but on the "minimum perceptible," which affords greater sensitivity and greater rapidity of investigation.

The Sloan perimetric light sense tester has been described in a previous article.[12] It is based on determination of the light threshold in several meridians of the visual field from center to periphery.

Davis [13] described a rough test for night vision testing as follows:

Mount on a post at the end of a level space 5 yards wide and 40 yards long and away from all artificial light, a black target on which is a movable white

8. Schonberg, A. L.: Plans for Inexpensive Improved Biophotometer, Mil. Surgeon **94**:308-311 (May) 1944.

9. Oldham, H.; Roberts, L. J.; MacLennan, K., and Schlutz, F. W.: Dark Adaptation of Children in Relation to Dietary Levels of Vitamin A, J. Pediat. **20**:740-752 (July) 1942.

10. Saubermann, G. V. C.: Ueber die Unterschiedsempfindlichkeit des dunkeladaptierten Auges, Ophthalmologica **104**:157-165 (Sept.) 1942.

11. Costi Garcia de Tunon, C.: Presentation of a New Umbralometer, Arch. Soc. oftal. hispano-am. **1**:114-122 (July) 1942.

12. Holmes, W. J.: Night Vision, Arch. Ophth. **30**:267-277 (Aug.) 1943.

13. Davis, W. T.: Military Ophthalmology, Am. J. Ophth. **27**:26-44 (Jan.) 1944.

strip, 6 by 24 inches. Mark off distances from the target at 5-yard intervals. After the person to be tested has been kept away from all artificial illumination for 25 minutes, direct him to walk slowly from the far end of the test area toward the target. The distance at which he is first able to identify correctly the position of the white strip is noted. While the person being tested is walking back for another trial, the white strip is changed. Several trials are made.

It is recommended that this test be performed on a dark night, before the moon has appeared.

Additional tests of dubious scientific, but possibly of some practical, value may be mentioned.

The "scratch test" consists in recording the number of scratch marks on the body of a subject who has hiked through a thick brush of cactus on a narrow, winding lane on a dark, moonless night.

The "self-preservation" test assesses the ability of a subject to emerge relatively unscathed after he has taken part in a game played with a heavy white medicine ball in a completely darkened gymnasium.

The "purgation test" is administered to persons who are suspected of malingering. A strong cathartic is administered in the evening and is so timed that a subject who reported inability to see clearly one night may, without his knowledge, be observed as he rushes for the toilet the next night, after taking the cathartic.

The "latrine test" consists in ordering suspected malingerers to cross in the dark a latrine trench across which a single plank has been laid. If the subject falls in, his disability is considered genuine.

Numerous attempts have been made to correlate vitamin A levels of the blood with the results of dark adaptation. Haig and Patek [14] found no correlation between vitamin A levels of the plasma and the parameters of dark adaptation in normal patients or in patients with cirrhosis of the liver. Steven,[15] however, reported that he found a high degree of correlation between the rise of visual thresholds and the fall of vitamin A levels of the blood. In a study of the amount of vitamin A in the blood and of the visual threshold measured with the Hecht-Shlaer adaptometer, Yarbrough and Dann [16] concluded that a single measurement of the visual threshold is not a reliable indicator of the vitamin

14. Haig, C., and Patek, A. J., Jr.: The Relation Between Dark Adaptation and the Level of Vitamin A in the Blood, J. Clin. Investigation **21**:377-383 (July) 1942.

15. Steven, D. M.: Experimental Human Vitamin A Deficiency: The Relation Between Dark Adaptation and Blood Vitamin A, Tr. Ophth. Soc. U. Kingdom **62**:259-275, 1942.

16. Yarbrough, M. D., and Dann, W. J.: Dark Adaptometer and Blood Vitamin A Measurements in a North Carolina Nutrition Survey, J. Nutrition **22**:597-607 (Dec.) 1941.

A content of the blood. Bodansky, Lewis and Haig [17] found that estimations of the vitamin A concentrations of the plasma were considerably more sensitive than tests for dark adaptation in the detection of deficiencies of vitamin A. However, they stated that occasionally abnormal values for dark adaptation are accompanied with normal vitamin A levels of the blood.

In addition to the work already cited, there is a voluminous Russian and German literature on the manifold methods of testing dark adaptation and night vision. The more recent German reports [18] contain repeated references to objective means of examination based on the phenomenon of optokinetic nystagmus. No details, however, are available of the technics that are employed.

An appraisal of these instruments leads to the conclusion that they are not sufficiently interchangeable or mechanically perfected to serve as diagnostic indexes for the assessment of a subject's total night visual capacity.

OBJECTIONS TO PRESENT METHOD OF TESTING

The chief shortcomings of the instruments described may be listed as follows: Many measure only the light threshold, and not the form threshold; on the other hand, others express only the form threshold, giving no indication of the light threshold. The tests for the most part are conducted in only one area of the visual field, rather than in several areas. The targets for the measurement of form threshold in most of the instruments are of one standard size, rather than of several graded sizes. The duration of stimulation of the retina is controlled in only a few instruments, and then only at one speed, rather than at several speeds. Central fixation is provided for in some of the instruments and left out entirely in others. Perception of colors is considered of great importance in some of the tests, and indeed forms the basis on which the particular machines were constructed but is excluded entirely from others. Some of the examinations are performed monocularly, others binocularly. The distances at which the instruments are placed from the eyes vary all the way from 14 inches (35.5 cm.) to 40 yards (36.5 meters).

The principal reason for this apparent confusion is the lack of agreement among investigators as to the real nature of the function to be tested and the even greater lack of uniformity regarding the proper means of testing it.

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17. Bodansky, O.; Lewis, J. M., and Haig, C.: The Comparative Value of the Blood Plasma Vitamin A Concentration and the Dark Adaptation as a Criterion of Vitamin A Deficiency, Science **94**:370-371 (Oct. 17) 1941.

18. Rieken, H., cited by Ohm, J.: Adaptationsprüfung mittels des optokinetischen Nystagmus bei Augenzittern der Bergleute, Arch. f. Ophth. **145**:31-45, 1942.

The scientific approach to these controversial issues must emanate from the fundamental concepts of anatomy, physiology and optics which govern night vision.

PHYSIOLOGIC CONSIDERATIONS

Even at the risk of being pedantic, the terms, "dark adaptation" and "night vision" are redefined, as their improper interpretation has frequently been responsible for erroneous deductions. Dark adaptation refers to the increase in the sensitivity of the eyes that occurs when one passes from bright light to darkness. Night vision constitutes the visual sensation that takes place when the eyes are already in a relatively high state of dark adaptation. Thus it becomes obvious that the two functions are not synonymous and that tests for one cannot be used as diagnostic indexes for the other. This statement has been corroborated by Behr,[19] Best [20] and Wessely,[21] who found no abnormalties in the course and end values of dark adaptation in clinically pronounced cases of night blindness. Birnbacher,[22] similarly, concluded that tests for dark adaptation were not sufficiently indicative to serve as a basis of judgement of the extent of impairment of night visual function.

Whether the tests should be carried out monocularly or binocularly has been answered by Allen,[23] who found that shading one eye depressed the sensitivity throughout the spectrum not only of the other eye but of the rest of the retina of the same eye, the maximum effect being obtained not in complete dark adaptation but with very dim light. Schumacher [24] further stated that only the dark apparatus has the faculty of summation of impressions of both eyes. An anatomic background for these conclusions was discovered by Frey,[25] who found centrifugal neural paths

19. Behr, C.: Das Verhalten und die diagnostische Bedeutung der Dunkeladaptation bei den verschiedenen Erkrankungen des Sehnervenstammes, Klin. Monatsbl. f. Augenh. **5**:193 and 449, 1915.

20. Best, F.: Demonstrationen zur Funktionprüfung des Auges, Ber. ü. d. Versamml. d deutsch. ophth. Gesellsch. **3**:201-204, 1918.

21. Wessely, K.: Ueber Störungen der Adaptation, Arch. f. Augenh. **81**:53, 1916.

22. Birnbacher, T.: Die epidemische Mangelhemeralopie, Abhandl. a. d. Augenh. u. Grenzgeb., 1927, no. 53, pp. 18-19.

23. Allen, cited by Duke-Elder, W. S.: Text-Book of Ophthalmology, St. Louis, C. V. Mosby Company, 1937, vol. 1, p. 952.

24. Schumacher, G.: Ueber das Verhalten der monokularen und binokularen Reizschwelle während der Dunkeladaptation des Tages-und Dämmerungsapparates, Acta ophth. **15**:5-59, 1937.

25. Frey, E.: Vergeichend-anatomische Untersuchungen über die basale optische Wurzel, die Commissura transversa Gudden und über eine Verbindung der Netzhaut mit dem vegetativen Gebiet Hypothalamus durch eine "dorsale hypothalamische Wurzel" des Nervus opticus bei Amnioten, Schweiz. Arch. f. Neurol. u. Psychiat. **39**:255, 1937; **40**:69, 1937.

between the central parts of the brain trunk and the retina. This fact suggests the possibility of a reciprocal relationship between the brain and the retinas of the two eyes and throws additional light on the importance of dark adaptation in the phenomena of contrasts.

The size of the test object in determinations of the form threshold is of great importance. According to recent reports,[26] an average-sized plane cannot be discerned much over 1,000 feet (300 meters) away on a dark night. This corresponds to a 20/400 image. Such an image has to stimulate a considerable number of rods in a fairly large retinal area in order for it to be perceived by the brain. The recognition of smaller objects offers even more of a problem, as it is well known that the rods, unlike the cones, are not connected with individual nerve fibers but are bunched together and produce an indistinct blurred image only by summation of several subliminal stimuli. Nevertheless, for the purpose of qualitative discrimination, it is deemed advisable to conduct tests of the form threshold with several progressively smaller targets.

The retinal area which is most sensitive in the dark-adapted state, and which therefore should receive the greatest attention, extends between 30 and 50 degrees from the fixation point. There is, however, another retinal area of equal importance in measurements conducted at low values of illumination. This is the so-called intermediate, or "transitional, zone," composed chiefly of rods, but also containing cones, and extending between 2 and 3 degrees from the fixation point. It is in this region that the retinal activities pass from the photopic to the scotopic mechanism. The study of this area is of practical significance as it functions at twilight, dusk and dawn, when both the scotopic and the photopic mechanisms may be called into play.

Central fixation is of undoubted value for measurements involving the light and form thresholds in multiple retinal areas at close range. It is also of consequence when the light and form thresholds are contrasted with each other in a definite sector of the retina. Both red light and self-luminous fixation devices may be utilized for this purpose. However, when the test object is large and is placed at considerable distance from the observer's eyes, it would seem more prudent to discard central fixation altogether and encourage the subject to scan the visual field with a series of quick, jerky movements, interrupted by short pauses, than to stare steadily at one or the other side of the object.

Measurements of the form threshold should also be conducted at distances ranging from 3 to 10 feet (0.9 to 3 meters) from the observer, utilizing larger targets.

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26. The Use of the Eyes at Night, United States Navy Department, Bureau of Medicine and Surgery, June 1939, pp. 660-665.

According to Michaelson, much valuable information may be gained by the routine investigations of both the light and the form sense. He found that patients with defective night vision have a poor minimum form sense. However, persons without defective night vision may also have a poor minimum form sense. When poor minimum light sense is associated with good minimum form sense, it indicates malingering.

The exact intensity of illumination at night is still a matter of controversy. According to Moon,[27] night vision can be considered to have supervened when the intensity reaches about 0.001 millilambert. For purposes of examination, instruments that furnish illumination ranging from 1 to 6 micromicrolamberts have been found adequate.

RECOMMENDED TECHNIC OF EXAMINATION

Preliminary Procedures.—Before the actual examination of the night visual faculty is undertaken, the following preliminary procedures should be carried out:

1. Inquiry into the past and family histories of the patient. This should include questions regarding hereditary and preexisting ocular diseases, previous gastrointestinal and metabolic disturbances, use of alcohol and drugs and all other factors which might have a bearing on the perception, conduction and interpretation of images at low intensities of illumination.

2. Determination of the age of the patient. It is well known that with advancing years, owing to senile changes in the lens alone, there are often increased absorption and retarded transmission of radiant energy.

3. A psychiatric appraisal of the subject. The importance of the willingness and eagerness to cooperate and an estimate of the reaction time of the nervous system in examinations of the scotopic state cannot be adequately emphasized and has already been alluded to in the first portion of this report. Indeed, the psychiatric examination is of such far reaching clinical significance that until a reliable objective method of testing is devised an impartial evaluation of night vision cannot be accurately made.

4. Examination of the photopic visual acuity of each eye for distance, with correction if such is worn. In this regard, it is felt that the patient who wears a correction for distance to improve his photopic vision should keep his glasses on while he is being tested for his scotopic ability. No amount of persuasion will make him believe, especially if he is wearing a strong correction, that his night vision will not be adversely affected by his being tested with his naked eyes. As a matter of strict fact, there is no conclusive experimental evidence that scotopic vision remains entirely

27. Moon, P.: The Scientific Basis of Illuminating Engineering, New York, McGraw-Hill Book Company, Inc., 1936.

unaltered when carried out in the absence of the magnifying or minifying effects of lenses worn during the photopic phase of seeing.

5. Careful examination of the external ocular segments, the media and the fundi of both eyes.

6. Estimation of the errors of refraction of each eye.

7. Preexposure of both eyes to a known intensity of light for a known length of time (e.g., to a brightness of 1,500 millilamberts for three minutes).

8. Dark adaptation for thirty minutes. This may be accomplished by the use of dark adapter red goggles for twenty-five minutes, followed by a five minute period in a completely darkened room, or, preferably, by staying in a completely dark chamber for the entire thirty minutes.

THE EXAMINATION PROPER

A systematic examination of a subject's night perception may then be made, according to the following technic:

1. Plotting of the entire course of dark adaptation. This is to include determination of

(a) the cone threshold,

(b) the transition time between the cone and the rod threshold,

(c) the rod threshold, and

(d) the final rod threshold level.

2. Determinations of the light threshold in at least four quadrants of the visual field, in retinal areas corresponding to 40 degrees from the central fixation object.

3. Determinations of the form threshold, in a manner similar to that outlined in 2.

4. Correlation of the light and form thresholds. The ratio thus obtained should be compared with a predetermined standard and may in some cases aid in the detection of malingering.

5. Determinations of the light threshold at several time intervals. Speeds of 1, 1/2, 1/5, 1/10, 1/20 and 1/40 second are recommended.

6. Determination of the form threshold at the transitional zone of the retina 2 to 3 degrees from the fixation object.

7. Determinations of the light threshold throughout at least 1 meridian of the visual field, from center to periphery (according to Sloan's technic).

8. Determination of the form threshold with a series of graded objects, beginning with an object corresponding to the 20/400 letter and substituting smaller objects in the successive tests.

9. Examinations conducted out of doors on a starlit, moonless night, according to Davis' technic or one of its modifications.

10. Serologic studies of the vitamin A concentrations of the blood plasma.

11. Further investigations, if such are indicated, in instances in which additional information is desired by the examiner. The procedures employed in these instances depend entirely on the examiner's ingenuity and on the circumstances bearing on the individual case. A few such tests which have been recommended, and might be put to use if desired, include (*a*) use of a longer adaptation time; (*b*) trial feedings with controlled quantities of vitamins A, B, C, and D; calcium, and placebo substances; (*c*) administration of such substances as oxygen, ephedrine, amphetamine and thyroid; (*d*) retests of night vision after the subject is exposed to a trial series of conditioned reflexes, and (*e*) the "cactus test" and other procedures.

12. One or more reexaminations of all subjects who failed on the first test, before their night vision is definitely declared unsatisfactory. Indeed, even subjects with superior abilities should be retested, and the results of the second examination should be recorded, as they are of more value than those of the first examination.

It is neither necessary nor desirable to carry out all these tests on every subject or to repeat the entire procedure when a candidate comes up for reexamination. Tests 1 to 6 will in most instances provide sufficient information to enable the examiner to classify his subject correctly as having superior, satisfactory or unsatisfactory night vision. The remaining tests are included for the purpose of providing an orderly method of examination, especially for subjects who possess highly developed night visual capacities and who have to be selected for specialized duties requiring such abilities.

During war, a study of the intricate problems of night vision is of practical significance in determinations of the suitability of men for night operations. In peacetime the subject will be of even greater practical importance, as the results of light and form threshold examinations will enable the ophthalmologist to suspect an incipient lesion of the posterior segment of the eye before irreversible changes in the fundus have taken place.

The establishment of universally accepted standards for the determination of the factors that constitute a person's ability to see in the dark is extremely desirable. Such a procedure would enable different observers in different parts of the world to accumulate extensive statistical data based on a uniform technic and expressed in uniform terminology and would lead to a better understanding of this important and relatively miscomprehended phase of ophthalmology.

SUMMARY

Comparisons were made of six devices used for investigating night vision. The correlation that existed among these devices was not sufficient to warrant their use interchangeably. A partial list of additional devices used for testing dark adaptation and night vision is appended, together with objections raised against them. A thorough, systematic method of examination based on physiologic principles for the study of the function of night vision is described and its uniform acceptance advocated.

45 Young Building.

REDUCTION OF REFLECTIONS

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OF ALL the technical advances to come out of the recent war, probably the most significant optically is the coating of lenses with reflection-reducing films. Now that coating has been made available to members of the profession, an appraisal of it is in order, for at present it has both limitations and important uses.

This development had its beginning as far back as 1892, when H. Dennis Taylor, a lens designer of England, observed that the iridescent tarnish which appeared on certain old camera lenses did not

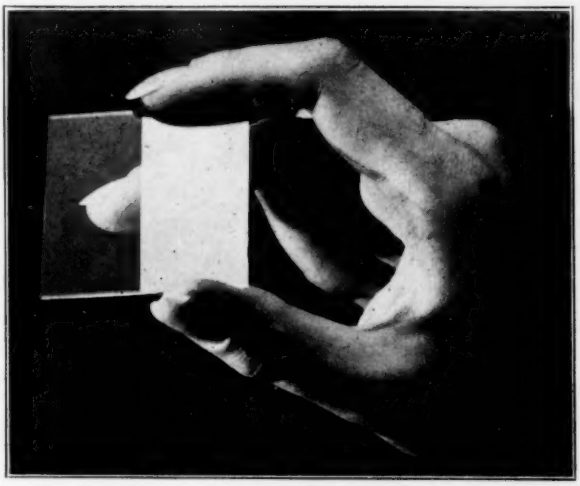

Fig. 1.—Left half of glass coated to reduce reflection.

reduce the light they transmitted, but increased it instead. The thin film [1] on these optical surfaces reduced reflections and increased the transmitted light by the amount of reduction of the reflections.

The physical conditions which produce zero reflection of monochromatic light are two. The film must equal in optical thickness one quarter of a wavelength of the incident light, and the refractive index of the film must be the geometric mean of the indexes of the first and second mediums. Under the most frequently encountered condi-

From the Department of Research and Education, the Univis Lens Company.

1. The metal oxides had been leached from the surface, leaving a thin layer of high silica glass of low density and, hence, low index of refraction.

tions (air to glass) the index of the intervening film should equal the square root of the index of the glass, and the film should be 0.000004 inch thick. The more nearly these conditions are satisfied, the more completely are reflections damped.

This damping is caused by destructive interference occurring at the two surfaces of the low index film, and, in accordance with the law of conservation of energy, the reduction in reflected energy is added to the transmitted beam.

Taylor developed methods of artificially tarnishing lenses, but the reduction in reflection was slight because the index of the film was not low enough for many glasses and the proper thickness was not appreciated. Other methods of approximating the requisite conditions were developed later, until, prior to the recent war, reflections were reduced by leaching lens surfaces with acids or their vapors, by coating with various stearate films and by whirling lenses so as to spread a thin layer of viscous fluid of low index evenly over the surface by centrifugal force. Some of these methods produced relatively durable surfaces and some relatively efficient ones, but none did both.

Since 1938 Strong, whose work was done at the California Institute of Technology, and Cartwright and Turner, whose major work was done at the Massachusetts Institute of Technology, have developed a process which combines the maximum efficiency with the greatest durability. This process, as utilized in optical lenses for the armed forces of this nation, consists in depositing a thin film of magnesium fluoride on optical surfaces in high vacuum and under considerable heat.

Lenses to be coated are treated with a detergent solution and then cleaned long and rigorously, so that no trace of foreign material or oxide remains on the surface. They are then racked in the top of a bell jar and heated to 400 + F. while the chamber of the bell jar is exhausted to an extreme vacuum of 4×10^{-6}, mechanical vacuum pumps and a high speed oil diffusion pump being used in series. Less than 1 part of air in 100,000,000 remains. After a protracted period under these conditions, the glass is degassed, and its raw substance is exposed. At this point pure magnesium fluoride, held in a crucible in the bottom of the bell jar, is heated by filaments of such high incandescence that they cannot be viewed with the unprotected eye. Under these conditions of heat and high vacuum, the magnesium fluoride vaporizes, and a molecular spray is deposited on the exposed under surface of the lenses. The technician, using a small fluorescent light source, judges the thickness of the film as it accumulates on the lenses by observing reflections from the surface of a monitor lens. As the deposition begins, the usual bright, white reflections from the lenses begin to dim and turn to a straw color. Then, growing dimmer all the time, they go through a succession of yellows, reds and reddish

blues, until when they reach a specific purplish tint the evaporation is stopped. At this point reflections are dimmed for all wavelengths but most completely dimmed for yellow (the one-quarter wavelength condition is exactly fulfilled for yellow of wavelength 555 millimicrons and less perfectly satisfied as the wavelengths of the other colors of the

Fig. 2.—Coating laboratory of the Univis Lens Company in operation.

spectrum differ from that of yellow). The slightly greater reflections of wavelengths at the two ends of the spectrum—the reds and violets—when blended produce the purplish tinge characteristic of the residual reflections from coated lenses. This is the condition of maximum reduction of reflections under ordinary daylight. After completion of the deposition, the lenses may be baked in vacuum for a considerable

time and then returned slowly to room temperature. The entire operation takes place in a laboratory in which conditions of temperature and relative humidity are controlled, and the air is Preciptron cleaned.

The result is a film almost exactly 0.000004 inch thick, which, when protected in optical instruments, is as permanent as the glass. On crown glass of index 1.52 the film reduces the amount of loss of light at each surface by a factor of 3. The reduction is not greater because magnesium fluoride has too high an index to satisfy perfectly the square root relationship and because in heterogeneous daylight the one-quarter wavelength condition cannot be satisfied for all wavelengths.

When light, traveling in air, impinges on the polished surface of crown glass of index 1.52, the loss is 4.2 per cent at each surface. Coating with magnesium fluoride reduces this loss to 1.3 per cent. In an optical system made up of many surfaces, the cumulative saving in light is considerable. In a regular binocular, consisting of ten optical surfaces, the following differences prevail:

	Uncoated Lens	Coated Lens
Percentage of light absorbed by glass	12	12
Percentage lost by reflections	33	10
Percentage of light transmitted	55	78

In systems with a greater number of surfaces the gain is even more striking.

The result is, in bright daylight, a reduction of ghost images due to interface reflections, and an increase in contrast and detail. In dim illumination this conservation of light often makes an optical system useful when before coating it would not have transmitted enough light for seeing. The tremendous value of this in extending, both at dusk and at dawn, the period of usefulness of photographic operations, observation devices and gunfire control systems can be appreciated. As a result, during World War II coating became mandatory for practically every optical system used by American fighting men. The creating of laboratories to treat the many millions of optical surfaces required was one of the production phenomena of the war just passed. Procurement of the high vacuum equipment was even permitted to compete with that of high vacuum equipment for the production of uranium 235, used in atomic bombs. In instrument optics, coating is an unqualified success, contributing much improvement, with no disadvantages.

But in ophthalmic optics one finds different and more exacting conditions. As a result one cannot, at this stage of development of the science, expect a repetition of the almost 100 per cent acceptance found in instrument optics. For ophthalmic use the coat must be rugged

indeed, for it is exposed to repeated cleaning and much abrasion. The reduction of reflections is only about 50 per cent, for the incidence of the light varies greatly, so that the one-quarter wavelength condition is not always entirely satisfied, even for yellow light. Scratches on a coated surface are more visible, for the light they reflect is more apparent against a dimly reflecting, coated surface than it would be against a brightly reflecting uncoated one. Furthermore, the gain in transmission, which is so important in a multisurface system, is practically meaningless in a two surface lens, in which loss of light is seldom a problem. Hence the coating of spectacles is of value only to the extent to which it can reduce reflections and at present can be recommended only when reflections are a problem.

Fig. 3.—Patient with left lens coated for reduction of reflections.

Reflections from glasses into the eyes of the wearer occur with every one who wears them. But it cannot be said to constitute a serious problem until the intensity of the reflections exceeds the tolerance of the patient. The intensity of reflections is highest when the prescription is of considerable power or when the wearer is in such a position that a window or bright source is behind and to the side. The tolerance of reflections will be lowest in neurasthenic and hypercritical patients. The result is a fair, though not yet accurately determined, proportion of patients who are consciously annoyed by reflections from their glasses and who are greatly relieved when these are substantially reduced.

This does not mean that the great body of patients who have learned to ignore reflections from their glasses would not welcome a reduction of the reflections, just as one, unconscious of a continuing noise, is relieved when the noise stops. But when coating has been available only for a limited time, a definite assertion to this effect cannot be made.

Reflections from glasses can do more than annoy the wearer. They can, and often do, conceal the eyes of the wearer from any one looking at him. This is detrimental enough in daily personal contacts, when the audience consists of one or a few. But to ministers, teachers and all who wear glasses when appearing before groups of people it is a serious impediment. Their expressions are masked, and the glare, coming and going as the speaker turns, is a disturbing thing to all the audience. Coating will considerably reduce such masking of the eyes.

In summary, it may be said that the coating available today through ophthalmic supply laboratories is durable, if not permanent, and reduces reflections substantially, although it does not extinguish them or make the glasses invisible. Coating is a new and important development which has reached a state of real usefulness, but not of perfection. As such, its judicious employment will increase the ways by which the profession serves and satisfies patients.

Univis Lens Company.

PRESERVATION OF CORNEAL TISSUE FOR TRANSPLANTATION

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WITH the advent of the corneal transplantation operation, there has been a gradual intensification of interest in the donor material to be used for this operation. The institution of the Eye Bank for Sight Restoration to supply adequate material for this operation is a step forward in the right direction, for this organization facilitates a rapid distribution of donor material to the proper place. However, the actual preservation of corneal material involves much more than meets the eye of the casual observer, and there is widespread misconception about this subject.

Contrary to the general opinion, corneal tissue is relatively short lived, and the best operative results in corneal transplantation are obtained when the material is fresh and used shortly after it is removed from the donor. Adult eyes after enucleation show normal transparency and no marked increase in corneal thickness due to edema for forty-eight to seventy-two hours, but thereafter the cornea becomes gradually and progressively edematous, thick and hazy. All these features contraindicate the use of this tissue as favorable donor material. Eyes removed from stillborn infants show more rapid loss of corneal transparency than do adult eyes, and consequently more care must be exercised in evaluating gross changes to determine whether the material is suitable for grafting. I have observed the corneas of stillborn infants become opaque and thick during the course of eighteen hours. The development of these characteristics, of course, foretells failure if such a cornea is used for transplantation. It often is not possible to tell whether corneal tissue is suitable for grafting until it is sectioned with the keratome, for such tissue may appear fairly transparent but on section may be found to have increased in thickness and possess a spongy character that will make it wholly unsuited for use in transplantation.

It was because of these varied problems and the general interest in this subject that a series of eyes were studied to determine the efficacy of various mediums that might be useful in the preservation of corneal tissue. The eyes used for study were obtained from rabbits.

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The question was raised as to whether or not the eye should be preserved intact or whether the cornea should be removed and suspended in solution or the fluid of the anterior chamber replaced with the preserving medium.

In removing the cornea and suspending it in solution, the difficult problem was encountered of satisfactorily cutting the corneal graft without adequate support. Moreover, corneal tissue rapidly became extremely edematous when suspended in any of the mediums used. A similar condition followed when the anterior chamber was drained and

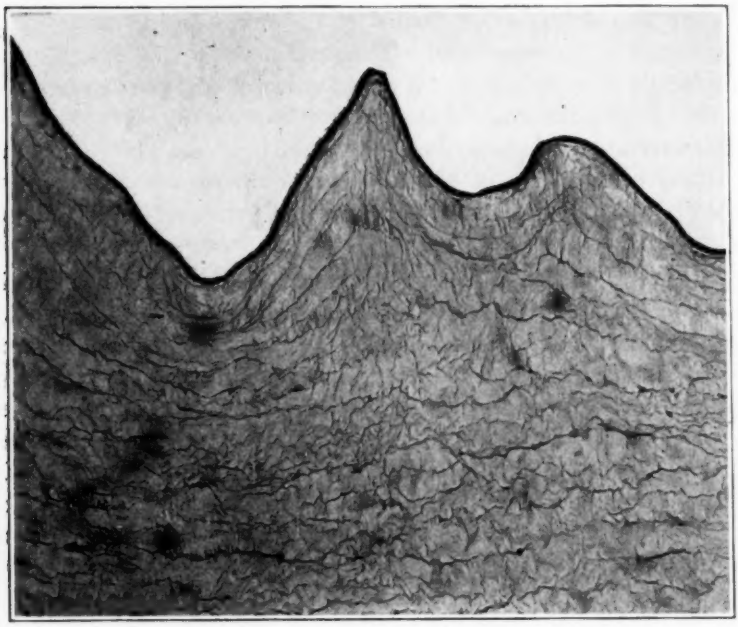

Fig. 1.—Microscopic section of edematous corneal tissue of an eye in which the fluid of the anterior chamber had been replaced with isotonic solution of sodium chloride and kept two weeks.

replaced with the preserving medium. Figure 1 shows a microscopic section of corneal tissue from a rabbit in which the anterior chamber was replaced with saline solution and two weeks was allowed to elapse. A similar thickening took place with all the solutions employed.

The following mediums were used: (1) isotonic solution of sodium chloride; (2) Hartmann's solution; (3) Hartmann's solution and 5 per cent dextrose; (4) plasma; (5) oxygenated plasma; (6) freezing agents, namely, (*a*) liquid nitrogen and (*b*) sodium pentothane (isopentane).

METHOD

The eyes used were removed under strictly antiseptic conditions. They were placed in small tubes containing 5 cc. of the preserving medium, this being enough to cover the specimen. These tubes were then kept in refrigeration at 3 C. At the designated times, the eyes were removed and corneal grafts obtained and transplanted to a normal eye.

Bacteriostatic agents were used early during these experiments, but because of the relatively short time the tissue could be kept this precaution was found to be unnecessary.

RESULTS

Suspension in Mediums.—Isotonic solution of sodium chloride was an adequate medium for keeping corneal tissue transparent for as long as three days. Uniformly transparent grafts were obtained when tissue was used up to the three day limit (fig. 2 *A*). By the fourth or fifth day the cornea was still fairly clear, but sections showed that the tissue was beginning to be spongy and thickened, and microscopic examination showed edema. When this material was used for grafting, the resultant

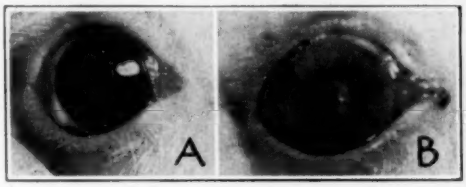

Fig. 2.—*A*, clear corneal graft. Donor material was kept for three days in isotonic solution of sodium chloride. *B*, corneal graft, showing clear area. Donor material had been kept for five days in isotonic solution of sodium chloride.

transplant in most cases was completely opaque. However, the opacity of this graft was not as thorough or as complete as that of a graft using material kept for one week. The former in most instances showed relatively clear areas, but these were not uniform and were present in only 10 of the 15 specimens studied. The grafts from the remaining 5 corneas had a diffusely hazy character, through which the detail of the fundus could not be seen. In the eyes that showed relatively clear areas of cornea, such as the tissue shown in figure 2*B*, the fundus could be observed, but the detail could not be clearly made out. Microscopic section of the graft shown in fig. 2 *B* revealed diffuse fibrosis which was not present in sections through the clearer area. This fibrosis did not involve all the layers of the cornea, as is apparent in comparing the microscopic pictures in figure 3*A* and *B*. It was generally noted at this point that corneas preserved in saline solution were clearer and of more normal thickness than tissue similarly preserved in plasma. A few specimens were kept as long as one month merely to study the

changes taking place in the tissue, and it was found that, although all corneas at this time were greatly thickened and hazy, those preserved in saline solution showed the lesser change from normal.

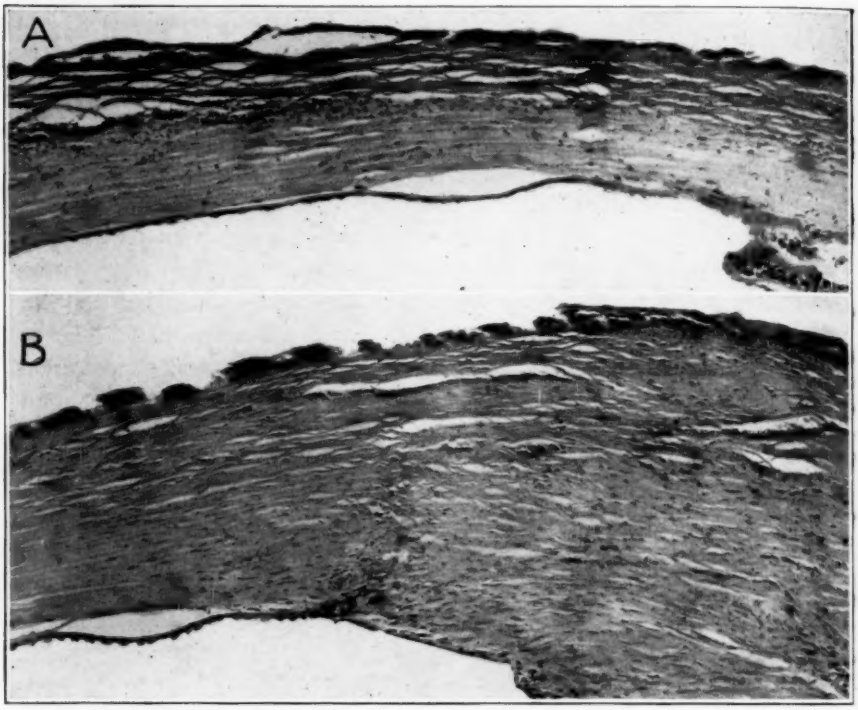

Fig. 3.—Microscopic sections of the corneal graft shown in figure 2 *B*. *A* is through the clearer area, and *B*, through the opaque area.

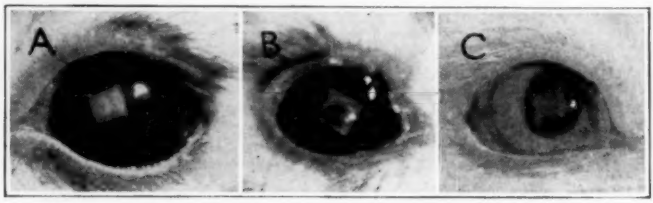

Fig. 4.—*A*, corneal graft, showing complete opacity. Donor material had been kept for one week in isotonic solution of sodium chloride. *B*, corneal graft, showing diffuse haziness. Donor material had been kept for five days in blood plasma. *C*, opaque corneal graft. Donor material had been kept for one week in blood plasma.

In eyes kept for one week the corneas repeatedly showed slight haziness but no great thickening, and when used for transplantation the grafts became completely opaque. The grafts from these eyes appeared to have a uniformly opaque character (fig. 4 *A*) and did not show any of

the clearer areas noted in those kept four or five days. In this series, 10 specimens were studied and used for transplants, and all showed the same results. After one week the haziness and thickening progressively increased, so that in two weeks the corneas were wholly unsuitable for grafting. Microscopic examination of this tissue showed pronounced separation of the stromal layers by edema.

Hartmann's solution, used alone or with the addition of 5 per cent dextrose, was a suitable medium for keeping the corneas clear for three to four days, but thereafter they became progressively hazy and thickened. In general, eyes kept in this medium followed the same course as that observed when isotonic solution of sodium chloride was used.

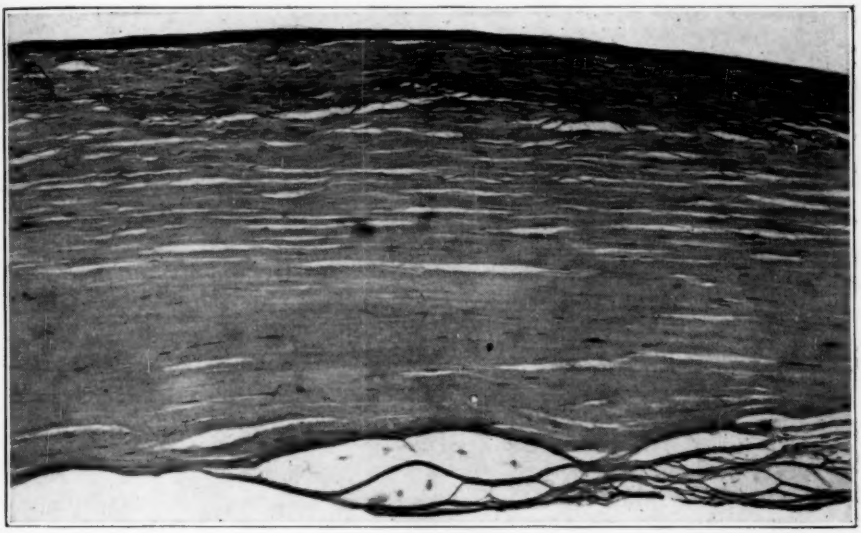

Fig. 5.—Microscopic section of the opaque corneal graft shown in figure 4 *C*. There are diffuse infiltration, fibrosis and hyalinization.

Plasma, either alone or oxygenated, was adequate to keep the cornea clear up to a period of three days, but after this time limit the material became useless for transplantation. At the end of four days the cornea began to thicken but still retained a reasonable amount of transparency, and microscopic examination showed edema. Use of this tissue for transplantation resulted in an opaque graft in most cases. Fifteen specimens were studied in this series, and 10 of them were uniformly opaque; but, again, the haziness of the graft was not extreme, and no detail of the fundus could be observed (fig. 4*B*). Only in 5 of these specimens were small clearer areas noted. At the end of one week the transparency of the corneas kept in such a medium was not greatly lessened but the tissue was beginning to thicken. Transplantation

at this time resulted in a completely opaque graft, as shown in figure 4 *C*. A microscopic section of such a graft (fig. 5) revealed diffuse fibrosis of all the layers, and showed much denser hyaline and fibrous changes than those seen in figure 3.

Freezing Method.—The freezing experiments were done in collaboration with Dr. Arnold Lazarow, of the department of anatomy of Western Reserve University. A small wire mesh container was used to place the eyes in the freezing medium. Liquid nitrogen was the agent used, which lowered the temperature to — 185 C. Eyes placed in this medium were frozen solid in a few seconds. Before the specimens were placed in the freezing solution, a 5 mm. trephine opening was made in the sclera, including the optic nerve, to allow for expansion. Otherwise, the cornea would have shown multiple fracture lines when the tissue returned to normal temperature. One series was used in which the eyes were frozen by merely placing them in the container immersed

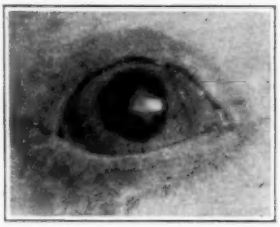

Fig. 6.—Opaque corneal graft, showing absorption along the borders and replacement with scar tissue. Donor material had been frozen in liquid nitrogen.

in the liquid nitrogen. Another series was prepared in which the eyes were first placed in a previously cooled small flask containing isopentane which caused the eyes to freeze more rapidly. This flask was then immersed in the liquid nitrogen. After freezing, the eyes were placed in a refrigerator compartment which kept the temperature at — 40 C.

When ready for use, the eyes were removed from the refrigerator, and approximately two hours was required for "thawing out." At the end of this time the cornea had returned to nearly normal transparency, but it had lost some of its normally firm consistency. This was true whether the eye was frozen directly in liquid nitrogen or immersed in the isopentane solution. Both gave the same results. When this material was used for corneal transplantation, the graft retained a reasonable amount of transparency for about one week but thereafter gradually became opaque (fig. 6). As illustrated in figure 6, the graft showed some absorption and replacement of the donor material with scar tissue. The opacity was dense, and microscopic section (fig. 7) revealed almost complete fibrosis of the graft.

CONCLUSIONS

From the preceding data, it is apparent that corneal tissue will remain clear and of normal thickness and can be used suitably for transplantation up to a period of three days. Thereafter the tissue becomes progressively hazy and thickened, being thus rendered unsuitable for grafting. After three days there may be areas of transplanted cornea that tend to retain transparency, but tissue kept for one week becomes uniformly opaque. For keeping corneal tissue clear, a solution may be used that is as nearly isotonic with the body fluids as possible—whether this be saline solution, Hartmann's solution or blood plasma. It is evident, however, that the tissue in question will not survive for long periods outside the body and retain its normal characteristics.

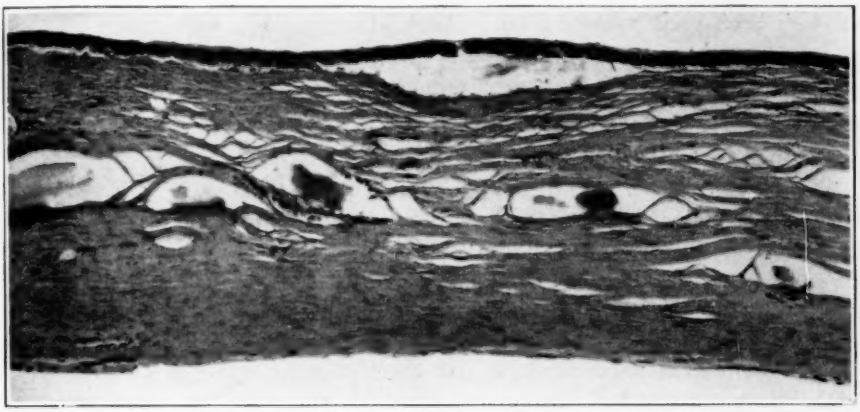

Fig. 7.—Microscopic section of the corneal graft seen in figure 6. There are infiltration, disorganization of the stromal layers and fibrosis.

After frozen corneal tissue returned to normal body temperatures, it regained its original transparency; but here, again, there had been some loss in the viability of the tissue, as it invariably became opaque with transplantation.

It can be concluded from this study that corneal tissue to be used for transplantation should be obtained from a fresh specimen and used within a relatively short period in order to obtain the best surgical results. In general it has been observed that these experimental data can be applied to clinical cases, and the general principles here set forth should be followed in the preservation of human tissue for corneal transplantation.

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Ophthalmologic Reviews

EDITED BY DR. FRANCIS HEED ADLER

METABOLISM OF THE RETINA

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DURING the past few years the interest in retinal metabolism has been greatly intensified. Many investigations were made on the retina as part of a war emergency program. Because of this practical interest in a narrow but important subdivision of ophthalmology, this survey of the literature was made.

A study of the metabolic processes in the retina has been the basis of much research, particularly within the last ten years. This is not surprising, as such work may have a double goal—first, to provide additional information on the problem of visual mechanisms and, second, inasmuch as the retina shows metabolic activity greater than that of almost any other tissue, to study the chain reactions of intermediate metabolism. The extensive literature, dealing with many phases of the problem, is difficult to put together into a single picture, and therefore one must present many observations alone and await further investigation to understand fully their significance. In this paper no attempt is made to discuss the mechanism of the visual pigments, although their reactions are certainly a part of retinal metabolism. The discussion is limited chiefly to carbohydrate metabolism, with reference to a possible fat and protein metabolism. It is to be remembered that the process observed in a complex organ such as the retina may represent the summation of metabolic processes connected with the visual mechanism, the transmission of impulses along nerve fibers and across the synapses and the basal metabolism of the cells involved.

METHODS AND MATERIAL

These studies were made on retinas obtained from the eyes of various animals, principally the frog, rat, rabbit and ox. In many cases unexplained species variation may add to the difficulty in comparing results. Studies of oxygen utilization, carbon dioxide production, aerobic and anaerobic glycolysis and ammonia produc-

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This survey was supported in part by a grant from the John and Mary R. Markle Foundation.

tion were made with the Warburg manometer, employing the entire retina, sliced or minced retinas, retinal extracts or, occasionally, special slices including only certain regions or layers of the retina. The effect of various added substrates or poisons, as well as the production of final or intermediate products, was determined with this method. The Thunberg method was employed for determination of dehydrogenases. Measurements of the p_H were usually made with the hydrogen electrode. Acetylcholine was determined by bioassay, using the magnitude of muscular contraction as compared with a standard. The effects of light and dark adaptation were found by illuminating one eye of an animal, the lids being held open and the eye irrigated, while the other eye was blindfolded to serve as the control, and then quickly placing the retinas in the manometer vessels. The effect of illuminating and darkening the vessels was also investigated.

Determinations on the human retina were limited to a few cases in which the eye was enucleated, usually for glaucoma or tumor, and to the indirect observations in which the effect of anoxia and carbon dioxide excess on the dark adaptation and the visual acuity of volunteer subjects was noted.

RESULTS

Hydrogen Ion Concentration.—The early work of Chodin [1] in 1878, and of Kühne [2] and Cahn,[3] shortly thereafter, showed little change in the slightly alkaline retina on exposure to light; yet Angelucci,[4] at about the same time, first demonstrated the shift toward the acid side on illumination, which fact has subsequently been often confirmed. Lodato,[5] in 1900, stated that the greatest acidification was given by light of short wavelength and also demonstrated how thermal, electrical or chemical irritation could produce acidity. Majima,[6] however, showed that yellow and green light were more effective. Re [7] produced acidity by stimulation of the optic tract. Quantitative studies by Nakashima [8]

1. Chodin, A.: Ueber die chemische Reaktion der Netzhaut und des Sehnerven, Sitzungsb. d. k. Akad. d. Wissensch. Math.-naturw. Cl. **76**:121, 1878.

2. Kühne, W.: Chemische Vorgänge in der Netzhaut, in Hermann, L.: Handbuch der Physiologie, Leipzig, F. C. W. Vogel, 1879, vol. 3, p. 234.

3. Cahn, A.: Zur physiologischen und pathologischen Chemie des Auges, Ztschr. f. physiol. Chem. **5**:213, 1881.

4. Angelucci, A.: Histologische Untersuchungen über das retinale Pigmentepithel der Wirbelthiere, Arch. f. Physiol., 1878, p. 353.

5. Lodato, G.: Imutamenti della retina sotto l'influenza della luce, dei colori e di altri agenti fisici e chimichi, con speciale riguardo alla reazione chimica: contributo alla fisiologia della retina, Arch. di ottal. **7**:335, 1900; abstracted, Klin. Monatsbl. f. Augenh. **38**:365, 1900.

6. Majima, K.: Studien über die Struktur der Sehzellen und der Pigmentepithelzellen der Froschnetzhaut, Arch. f. Ophth. **115**:286, 1925.

7. Re, F.: Sulle modificazioni fisiche e chimiche della retina per l'eccitazione elettrica dell'encefalo, mesencefalo e chiasma, Arch. di ottal. **12**:147, 1904; abstracted, Arch. d'opht. **26**:123, 1906.

8. Nakashima, M.: Beiträge zur Kenntnis des Sehpurpurs, XIII. Internationaler Ophthalmologenkongress, Amsterdam, 1929; abstracted, Zentralbl. f. d. ges. Ophth. **22**:772, 1930.

showed the p_H of the dark-adapted retina to be about 7.3 and that of the light-adapted retina to be about 7.0.

That this change may be related to the activity of the visual cells rather than of the nerve elements and may vary with the type of cell was shown in 1937 by von Studnitz,[9] who found no change in the p_H of the guinea pig retina, which contains only rods, while the cat and fish retinas, which contain also cones, showed a shift to the acid side. The acidity increased with time, corresponding to the regeneration of visual substances. The production of acid increased with elevation in temperature, as well as with greater intensity of light. After fifteen minutes of illumination acidification decreased (probably through the exhaustion of visual substance reserves) but rose again after twenty to twenty-five minutes (probably because of supplementary visual substances). The curve of acid production at different wavelengths of light for the reptile corresponds to the absorption curve of the cone substance, being greatest with yellow light. Von Studnitz' further work[10] showed little change in p_H on illuminating the retinas of selachians and cephalopods, which contain only rods. He expressed the belief that acidification of the retina leads to contraction of the cones and expansion of pigment. Dittler,[11] in 1907, showed that an aqueous extract of a light-adapted retina caused the contraction of cones in a dark-adapted retina, similar to the stimulation of light.

Organic Phosphate.—A study of the phosphoric acid and phosphoric esters in the retina, particularly because of their importance in intermediate carbohydrate metabolism, may provide important information concerning the sources of energy for visual processes. Lange and Simon,[12] in 1922, showed that frog retina contains 0.08 per cent phosphoric acid. A phosphate ester apparently present in the outer segments of the rods of the frog and carp was hydrolyzed in alkaline solution into phosphoric acid and an organic substance. An increase of phosphoric acid in the vitreous of a removed eye was noted on high illumination; a partial reformation of the phosphate ester took place only if the retina was removed with the pigment epithelium; yet no phosphate was obtained from the pigment epithelium alone on illumination. The organic phosphate compound was not hexose phosphate, but probably

9. von Studnitz, G.: Die retinale Säurebildung, Arch. f. d. ges. Physiol. **238**:802, 1937.

10. von Studnitz, G.: Ueber die chemische Reaktion der Selachier- und Cephalopodenretina, Ztschr. f. vergl. Physiol. **19**:615, 1933.

11. Dittler, R.: Ueber die chemische Reaktion der isolierten Froschnetzhaut, Arch. f. d. ges. Physiol. **120**:44, 1907.

12. Lange, H., and Simon, M.: Ueber Phosphorsäureausscheidung der Netzhaut bei Belichtung, Ztschr. f. physiol. Chem. **120**:1, 1922.

phosphocreatine. Tawara [13] found two types of organic phosphate in the retina which liberated inorganic phosphate on illumination, one of which appeared to be phosphocreatine, the other a soluble phosphate ester. Kuzuya,[14] also working with the rabbit retina, demonstrated an acid-soluble and an acid-insoluble phosphate compound. He also investigated the changes in the amount of these different phosphate fractions with the growth of the rabbit.[15]

Nakashima and Arata [16] considered the possibility that phosphoric acid arose from the splitting of phosphocreatine in a manner analogous to that occurring in muscle but presented evidence against the photolysis of phosphocreatine. They showed that it is the Kjeldahl nitrogen (choline, carnosine) which increases on illumination and proposed the theory that phosphoric acid arises through the photolysis of retinal lipids. They stated the belief that phosphocreatine nitrogen, which increased with damage to the tissue and was inhibited by light, occurred through the autolysis of the retina.

Takamatsu [17] demonstrated that the isolated retinas of frogs and white rats produced phosphoric acid in Ringer's solution (isotonic solution of three chlorides U.S.P.) even in the dark, probably as the result of autolysis. Within limits, the increased production of phosphoric acid on illumination varied with length of exposure. That this process was reversible was shown by the fact that on darkening the once lighted retina production of phosphoric acid could again be demonstrated on illumination. Illumination of the retina of the white rat produced a reduction of phosphatide content. He further showed [18] that in frogs and rabbits poisons which produced acute amaurosis or amblyopia, such as methyl alcohol and quinine, decreased the phosphate ester content.

13. Tawara, M.: The Effect of Light upon the Phosphoric Acid Fraction of the Retina, Acta Soc. ophth. jap. **42**:1503, 1938; abstracted, p. 106.

14. Kuzuya, N.: Veränderung des Gehalts von verschiedenen Phosphorsäurefraktionen in Hell- und Dunkelnetzhaut, Acta Soc. ophth. jap. **41**:637, 1937; abstracted, p. 51.

15. Kuzuya, N.: Veränderung des Gehaltes der Netzhaut an verschiedenen Phosphorsäurefraktionen mit dem Wachstum, Acta Soc. ophth. jap. **41**:335, 1937; abstracted, p. 28.

16. Nakashima, M., and Arata, Y.: Azotometria der Netzhaut, Acta Soc. ophth. jap. **40**: 1586, 1936; abstracted, p. 97.

17. Takamatsu, T.: Photochemische Studien der Netzhaut: II. Ueber die Phosphorsäurebildung und die Phosphatidveränderung der Netzhaut bei Lichtung, Acta Soc. ophth. jap. **38**:1035, 1934; abstracted, p. 71.

18. Takamatsu, T.: Photochemische Studien der Netzhaut: III. Ueber den Einfluss der Gifte (Methylalkohol, Chinin) auf die Phosphorsäurebildung der Netzhaut bei Belichtung, Acta Soc. ophth. jap. **39**:598, 1935; abstracted, p. 54.

Von Studnitz [19] assumed that light decomposed the cone substance, with the production of phosphoric acid, expansion of pigment and contraction of cones, and as proof he showed that the injection of this acid into the dark-adapted retina produced a configuration of the cones and pigment for light, while injection of alkali into light-adapted retinas resulted in a configuration for the dark. There was a parallel change in the light absorption curves with injection of acid and of alkali. He expressed the belief that the cones alone show motility.

The increase in electrical conductivity of a solution of visual purple in the light and the decrease in the dark, as measured by Lasareff,[20] was probably due to the reversible hydrolysis of organic phosphate.

Evidence would indicate, however, that the acid reaction on illumination previously mentioned is probably due to the production of lactic acid in glycolysis rather than to the aforementioned liberation of phosphoric acid.

Oxidation-Reduction Potential.—Nakashima [21] found that the oxidation-reduction potential of suspensions of frog retinas increased on illumination and decreased in the dark, while he and Hayashi [22] showed that at the same time the consumption of oxygen was unchanged. Iron, enzymes and lipid apparently took part in the transfer of electrons, as the potential was decreased by potassium cyanide and the prolonged action of toluene and was increased by iron salts. The change did not depend on the presence of visual purple.

Respiration and Glycolysis.—The unique respiratory activity of the retina has led to its extensive study. Warburg,[23] in 1927, showed that the retina had the highest rate of respiration and of anaerobic glycolysis of any tissue studied and an extremely high anaerobic glycolysis, which even surpassed that of most tumors. Kubowitz,[24] Negelein [25] and

19. von Studnitz, G.: Vom Energieumsatz in der Netzhaut, Naturwissenschaften **22**:193, 1934.

20. Lasareff, P.: Sur le changement de la conductibilité électrique du pourpre visuel au cours de l'éclairge, Compt. rend. Acad. d. sc. **181**:476, 1925.

21. Nakashima, M.: Ueber das Oxydations-Reduktions-Potential der Netzhaut, Ber. ü. d. Versamml. d. deutsch. ophth. Gesellsch. **47**:369, 1929.

22. Nakashima, M., and Hayashi, K.: Sur le potentiel d'oxydo-réduction de la rétine, J. Biochem. **17**:315, 1933.

23. Warburg, O.: Ueber die Klassifizierung tierischer Gewebe nach ihrem Stoffwechsel, Biochem. Ztschr. **184**:484, 1927.

24. Kubowitz, F.: Stoffwechsel der Froschnetzhaut bei verschiedenen Temperaturen und Bemerkung über den Meyerhofquotienten bei verschiedenen Temperaturen, Biochem. Ztschr. **204**:475, 1929.

25. Negelein, E.: Ueber die glykolytische Wirkung embryonalen Gewebes, Biochem. Ztschr. **165**:122, 1925.

Oguchi,[26] working with frogs, and Nakashima,[27] using fish, demonstrated that in these cold-blooded animals the anaerobic glycolysis increased with the temperature and was much greater than the aerobic glycolysis up to 37 C., after which the aerobic glycolysis predominated. This effect of temperature was confirmed for mammalian and avian retinas by Warburg and associates,[28] Krebs [29] and Schmitz-Moormann.[30] Oguchi [31] compared the rates of respiration and glycolysis in birds, fish and frogs and found values for both to be highest in birds and least in frogs. Warburg and associates [28] suggested that the lactic acid produced aerobically from glucose was the result of trauma to the retina. In studying the lactic acid production of the retina of growing chickens, Tamiya [32] obtained the highest values during the period of growth and a decrease on maturity.

There appears to be a distinct difference between warm-blooded and cold-blooded animals in the effect of light on respiration and glycolysis. Kiyohara [33] reported that the dark-adapted retina of the toad took up 3.9 cu. mm. of oxygen per milligram hour, while the light-adapted retina took up 2.8 cu. mm. Jongbloed and Noyons [34] showed the oxygen consumption to be 26.5 per cent higher and the carbon dioxide production 25 per cent higher in dark-adapted than in light-adapted retinas of the frog. Similar results were obtained in the frog by Noyons and Wier-

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26. Oguchi, T.: Ueber den Stoffwechsel der Netzhaut: II. Der Stoffwechsel der Netzhaut der Reptilien; der Stoffwechsel der Netzhaut nach dem Tode des Froschen, Acta Soc. ophth. jap. **36**:1702, 1932.

27. Nakashima, M.: Stoffwechsel der Fischnetzhaut bei verschiedenen Temperaturen, Biochem. Ztschr. **204**:479, 1929.

28. Warburg, O.; Posener, K., and Negelein, E.: Ueber den Stoffwechsel der Carcinomzelle, Biochem. Ztschr. **152**:308, 1924.

29. Krebs, H. A.: Ueber den Stoffwechsel der Netzhaut, Biochem. Ztschr. **189**:57, 1927.

30. Schmitz-Moormann, P.: Ueber den Glykogengehalt der Retina und seine Beziehungen zur Zapfenkontraktion, Klin. Monatsbl. f. Augenh. **78**:69, 1927.

31. Oguchi, T.: Ueber den Stoffwechsel der Netzhaut: I. Der physiologische Stoffwechsel der Netzhaut der verschiedenen Tierarten; der Stoffwechsel der Netzhaut nach dem Tode der Tiere, Acta Soc. ophth. jap. **36**:1203, 1932.

32. Tamiya, C.: Ueber den Stoffwechsel der Netzhaut in verschiedenen Stadien ihrer Entwickelung, Biochem. Ztschr. **189**: 114, 1927.

33. Kiyohara, K.: Ueber die Wirkung der Strahlen verschiedener Wellenlängen auf die Säuerstoffatmung der Netzhaut, Nagasaki Igakkai Zassi **9**:730, 1931; abstracted, p. 735.

34. Jongbloed, J., and Noyons, A. K. M.: Säuerstoffverbrauch und Kohlendioxydeproduktion der Freschretina bei Dunkelheit und bei Licht, Ztschr. f. Biol. **97**:399, 1936.

sma [35] and Lindeman.[36] Ikemune [37] found a 10 per cent greater carbon dioxide production from the frog retina in the dark than on illumination and noted that the production was greater for longer periods of dark adaptation. He [38] reported that the glucose concentration of light-adapted retinas averaged 91 mg. per hundred cubic centimeters, while for dark-adapted retinas it averaged 20 to 79 mg. per hundred cubic centimeters. He interpreted these results as showing that the resynthesis of visual purple in the dark occurred with the energy of glucose metabolism and that the increase in carbon dioxide production was related to the increase in glycolysis.

On the other hand, Galante [39] found that light increased the oxygen consumption of the dove and sparrow retina, and Takano [40] demonstrated that in the rat the rate of respiration, as well as the aerobic glycolysis, increased on illumination of the dark-adapted retina. He [41] found that small differences in the duration, intensity or color of the light had no effect on the change. Yet, also working with the rat, Campos [42] obtained higher oxygen consumption in the dark-adapted than in the light-adapted retina. Kodama [43] compared the respiratory rate in vessels in the light and in the dark, perhaps a different matter than comparing the respiratory activity of light-adapted and of dark-adapted eyes, and found that the oxygen consumption and aerobic glycolysis were much greater in the dark than in the light for the first thirty minutes but then fell, approaching that of the retina in the light.

35. Noyons, A. K. M., and Wiersma, C. A. G.: L'influence de la lumière sur la consommation d'oxygène de la rétine de l'œil de grenouille, Acta brev. Neerland **3**:156, 1933.

36. Lindeman, V. F.: The Respiratory Metabolism of the Frog Retina, Physiol. Zoöl. **13**:411, 1940.

37. Ikemune, I.: Einfluss des Lichtes auf die CO_2-Produktion der Netzhaut, Okayama-Igakkai-Zasshi **51**:529, 1939; abstracted, p. 538.

38. Ikemune, I.: Der Einfluss des Lichtes auf die Glykolyse in der Froschnetzhaut, Okayama-Igakkai-Zasshi **51**:539, 1939; abstracted, p. 543; Der Einfluss des Lichtes auf die Glykolyse in der Froschnetzhaut, Jap. J. M. Sc. III, Biophysics **5**:90, 1938.

39. Galante, E.: L'azione dell'eccitamento retinico sul ricambio gassoso, Ann. di clin. med. **20**:79, 1930.

40. Takano, M.: Ueber die Gewebsatmung der Netzhaut der Ratte, Acta Soc. ophth. jap. **38**:1307, 1934; abstracted, p. 85.

41. Takano, M.: Ueber die Gewebsatmung der Netzhaut der Ratte: II. Ueber die Einflüsse der kurzen Beleuchtung des farblosen Lichtes und der dauernden Beleuchtung des farbigen Lichtes auf die Gewebsatmung und aerobe Glykolyse der Netzhaut, Acta Soc. ophth. jap. **39**:162, 1935; abstracted, p. 17.

42. Campos, R.: Ricerche sul ricambo della retina, Ann. di ottal. e clin. ocul. **64**:456, 538 and 577, 1936.

43. Kodama, S.: Studien über den Gaswechsel der Netzhaut der Ratte, Tohoku J. Exper. Med. **28**:423, 1936.

The oxygen consumption was not proportional to the intensity of the light. In colored light the oxygen consumption and aerobic glycolysis were greatest in red, less in green and least in blue light. In the dark, in dextrose-free Ringer's solution the oxygen consumption was high but fell rapidly to zero. In 0.1 per cent dextrose the oxygen consumption was high at first but fell rapidly to a fifth of its original value, and the aerobic glycolysis was high and decreased but little. In 0.4 per cent dextrose the oxygen consumption and aerobic glycolysis were comparatively low at the start and decreased only slightly. The anaerobic glycolysis was equally high in Ringer's solution containing 0.1, 0.2 and 0.4 per cent dextrose.

Working with the peripheral and central parts of monkey eyes, Campos [44] showed that both parts of the lighted retina showed less oxygen consumption than the dark-adapted retina, the values rising during the experiment and approaching the value for the dark-adapted retina. Glycolysis of the macula of the illuminated eye was less than that of the dark-adapted eye, while the peripheral parts showed no difference on illumination. Campos [42] measured the exchange of gases in human eyes removed six to ten days after injury and development of glaucoma. There was a high rate of respiration and of aerobic and anaerobic glycolysis, particularly the former. There was no excess of glycolysis, and the Pasteur effect was low or absent. The peripheral retina showed more active respiration than the macula except in cases of absolute glaucoma. He also examined the retinas of albino rats and found slightly more active respiration but definitely lower aerobic glycolysis than in pigmented retinas.

Anoxia.—Santoni [45] noted the effect of interrupting retinal circulation by ligating the entire orbital contents of rabbits and rats for fifteen to ninety minutes. He found that the oxidizing power increased after interruption for fifteen to thirty minutes but decreased after sixty to ninety minutes. De Crecchio [46] produced anoxia by compressing the globe of rabbits for thirty to one hundred and eighty minutes; anaerobic glycolysis was decreased after sixty minutes but increased after ninety or one hundred and eighty minutes. They expressed the belief that the decrease in glycolysis and the increased respiratory rate indicated degenerative changes as a result of ischemia, with the freeing of substances such as fats.

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44. Campos, R.: L'azione della luce sulla respirazione e sulla glicolise della retina, Boll. Soc. ital. di biol. sper. **11**:320, 1936.

45. Santoni, A.: Il ricambio della retina dopo interruzione della circolazione retinica, Ann. di ottal. e clin. ocul. **67**:299, 1939.

46. de Crecchio, A.: Il recambio della retina dopo compressione del bulbo, Ann. di ottal. e clin. ocul. **67**:739, 1939; abstracted, Arch. Ophth. **24**:1016 (Nov.) 1940.

The effect of anoxia in the human retina has been studied by many investigators. McFarland and Evans,[47] Gellhorn,[48] McDonald and Adler[49] and McFarland and Halperin[50] proved that lack of oxygen, excess of carbon dioxide or hyperpnea decreased visual acuity and dark adaptation. McFarland and Forbes[51] showed a similar effect of hypoglycemia. Vitamin A deficiency did not alter the effect of lack of oxygen. It undoubtedly acts by a different mechanism. It is probable that these changes were not concerned with the photochemical substances but involved the neural elements of the retina. In relation to avitaminosis A, however, de Leonibus[52] found that in albino rats placed on a deficiency diet until keratomalacia developed there was no change in oxygen consumption but that glycolysis was 8.6 per cent higher in the avitaminotic animals.

With atrophy of the retina produced experimentally by cutting the optic nerve in cats, Adler[53] showed there was an increased concentration of sugar in the vitreous. The glycolytic activity of the atrophied retinas, however, was decreased. In this manner the hypothesis that the low concentration of sugar in the vitreous is due to the high rate of glycolysis in the normal retina was confirmed. Craig and Beecher[54] observed that twice as much lactic acid was produced by the rat retina in phosphate as in bicarbonate buffer. In phosphate buffer there was a 38 per cent lower rate of respiration in 10 per cent oxygen and a 51 per cent lower respiratory rate in 5 per cent oxygen than in 100 per cent oxygen. The rates of respiration and glycolysis showed a reciprocal relationship to each other as the oxygen tension varied. In bicar-

47. McFarland, R. A., and Evans, J. N.: Alterations in Dark Adaptation Under Reduced Oxygen Tensions, Am. J. Physiol. **127**:37, 1939.

48. Gellhorn, E.: The Effect of O_2 Lack, Variations in the CO_2-Content of the Inspired Air, and Hyperpnea on Visual Intensity Discrimination, Am. J. Physiol. **115**:679, 1936.

49. McDonald, R., and Adler, F. H.: Effect of Anoxemia on the Dark Adaptation of the Normal and of the Vitamin A-Deficient Subject, Arch. Ophth. **22**: 980 (Dec.) 1939.

50. McFarland, R. A., and Halperin, M. H.: The Relation Between Foveal Visual Acuity and Illumination Under Reduced Oxygen Tension, J. Gen. Physiol. **23**:613, 1940.

51. McFarland, R. A., and Forbes, W. H.: Effects of Variation in the Concentration of Oxygen and of Glucose on Dark Adaptation, J. Gen. Physiol. **24**: 69, 1940.

52. de Leonibus, F.: Il ricambio della retina in avitaminosi A, Ann. di ottal. e clin. ocul. **67**:512, 1939.

53. Adler, F. H.: The Metabolism of the Retina: Further Notes, Arch. Ophth. **6**:901 (Dec.) 1931.

54. Craig, F. N., and Beecher, H. K.: The Effect of Low Oxygen Tension on Tissue Metabolism (Retina), J. Gen. Physiol. **26**:467, 1943.

bonate buffer, on the other hand, there was no sign of change in respiration with the oxygen tension lowered from 95 to 5 per cent, but glycolysis was increased nearly to anaerobic levels. Dickens and Greville [55] found that the rat retina, as well as the brain, oxidizes fructose strongly, although their earlier work [56] would indicate that in the case of the retina there is not an intermediate conversion into lactic acid, as they noticed negligible production of lactic acid from fructose. Chase and Hagan [57] proved that lack of oxygen does not alter the changes in the absorption spectrum of visual purple, thus giving further evidence that lack of oxygen affects only the neural elements of the retina.

General Metabolism.—Much information about normal retinal metabolism, as well as facts concerning pathologic conditions, has been gained by studying the effect of various poisons on metabolic changes. Holmes [58] and Lenti [59] showed that fluoride inhibited lactic acid formation from glucose, prevented the disappearance of inorganic phosphate and allowed no accumulation of phosphate esters, thus indicating that fluoride inhibits the first stage of glucose breakdown. Dickens and Greville [56b] noted that the inhibition of anaerobic glycolysis in a tissue parallels the magnitude of the glycolysis, and thus retina, with the highest glycolytic activity, was inhibited by less than 1 millimol of fluoride. Kerly and Bourne [60] found that in fluoride-poisoned extracts there was some formation of an ester which was hydrolyzed with difficulty from glucose and that its formation was increased by addition of pyruvic acid.

Lenti [59] also showed that a two-hundreth molar solution of iodoacetate inhibited glycolysis but that phlorhizin did not. On the contrary, de

55. Dickens, F., and Greville, G. D.: The Metabolism of Normal and Tumour Tissue: III. Respiration in Fructose and in Sugar-Free Media, Biochem. J. **27**:832, 1933.

56. Dickens, F., and Greville, G. D.: (*a*) The Metabolism of Normal and Tumour Tissue: VI. The Conversion of Fructose and Glucose to Lactic Acid by Embryonic Tissue, Biochem. J. **26**:1251, 1932; (*b*) VII. The Anaerobic Conversion of Fructose into Lactic Acid by Tumour and Adult Normal Tissues, ibid. **26**:1546, 1932.

57. Chase, A. M., and Hagan, W. H.: The Photochemical and Thermal Reactions of Visual Purple in Absence of Oxygen, J. Cell. & Comp. Physiol. **21**:65, 1943.

58. Holmes, B. E.: Inhibition by Fluoride of Glucose Breakdown in Tumour Tissue and Retina Extracts, Biochem. J. **34**:926, 1940.

59. Lenti, C.: Glycolysis in the Retina, Arch. di sc. biol. **25**:455, 1939; abstracted, Chem. Abstr. **34**:5903, 1940.

60. Kerly, M., and Bourne, M. C.: Glycolysis in Retinal Extracts, Biochem. J. **34**:563, 1940.

Conciliis [61] found that 0.02 to 0.01 millimol of phlorhizin had a strong inhibiting action on glycolysis, proportional to the concentration; there was little effect on the respiration, the action apparently being specific for glycolysis. Bisulfite and hydrazine inhibited glycolysis without the formation of methylglyoxal, triose or pyruvic acid. Süllmann and Vos [62] found phosphorylation and lactic acid formation are inhibited by glyceraldehyde and one-fortieth molar maleic acid. Kerly and Bourne [60] and Lenti [59] also observed the inhibitory effect on glycolysis of glyceraldehyde. Greville [63] noticed that in tissue with pure carbohydrate respiration, such as the retina, the respiration was inhibited by malonate but fumarate only partially relieved the inhibition.

Oguchi [64] showed that poisons, such as methyl alcohol, quinine and illuminating gas, which injure vision, also reduce the oxygen consumption 25 to 50 per cent in vitro. Wolff [65] reported that quinine if injected into the vitreous, and thus brought in direct contact with the retina, rapidly inhibited respiration but that subcutaneous injections did not inhibit oxygen consumption, even though complete amaurosis occurred. Only after repeated doses was any effect noted. Califaro [66] demonstrated how retinal glycolysis was inhibited by the agents which inhibit muscular glycolysis. Oguchi [67] showed that, while after the injection of 0.1 mg. of thyroxin per hundred grams of body weight the respiratory activity of the retina increased, the injection of one-tenth this amount produced a fall in the respiratory rate up to 20 per cent and a fall in glycolysis up to 30 per cent.

For the rat retina Laser [68] showed that carbon monoxide did not inhibit the oxygen uptake even in high concentration; however, it inhibits the Pasteur effect, aerobic equaling anaerobic glycolysis.

61. de Conciliis, N.: Ricerche sulla fosfatasi retinica, Sperimentale, Arch. di biol. **88**:793, 1934.

62. Süllmann, H., and Vos, T. A.: Der glykolytische Kohlenhydrataffau in Extraken der Retina, Enzymologia **6**:246, 1939.

63. Greville, G. D.: Fumarate and Tissue Respiration: I. The Effect of Dicarboxylic Acids on the Oxygen Consumption, Biochem. J. **30**:877, 1936.

64. Oguchi, T.: Ueber den Stoffwechsel der Netzhaut: IV. Ueber den Einfluss der Gifte (Methylalcohol, Chinin und Leuchtgas) auf den Stoffwechsel der Netzhaut, Acta Soc. ophth. jap. **36**:1997, 1932; abstracted, p. 155.

65. Wolff, E.: The Effect of Quinine on the Oxygen Consumption of the Dog's Retina, Tr. Ophth. Soc. U. Kingdom **56**:162, 1936.

66. Califaro, L.: Ricerche sulla glicolisi della retina, Atti d. Accad. Lincei **25**:93, 1937.

67. Oguchi, T.: Ueber den Stoffwechsel der Netzhaut: V. Ueber den Einfluss des Thyroxins auf den Stoffwechsel der Netzhaut, Acta Soc. ophth. jap. **37**:103, 1933; abstracted, p. 6; VI. Weiteres über den Einfluss des Thyroxins auf den Stoffwechsel der Netzhaut, ibid. **37**:956, 1933; abstracted, p. 72.

68. Laser, H.: Tissue Metabolism Under the Influence of Carbon Monoxide, Biochem. J. **31**:1677, 1937.

Elliott and Baker [69] found that the oxidation-reduction potential indicator 2,6-dichlorophenolindophenol in 1.3×10^{-3} concentration produced almost complete inhibition of respiration in the presence or absence of dextrose. According to Oyama,[70] the optimum p_H for respiration was 8.0 to 8.5. He also showed that the oxygen consumption of the temporal and that of the nasal half of the retina were the same. Between p_H 6.88 and 7.88 he found that the oxygen consumption increased with increasing alkalinity.[71]

The respiratory rate of rat retina was about twice as high in bicarbonate Ringer's solution as in phosphate Ringer's solution. Laser [72] also found that hydrocyanic acid inhibited the respiration of the retina in phosphate Ringer's but not in bicarbonate Ringer's solution. Craig and Beecher [73] observed that the metabolism of rat retina was sensitive to the concentration of the carbon dioxide–bicarbonate buffer system. Increasing the carbon dioxide concentration from 1 to 5 per cent at constant p_H almost doubled both the oxygen consumption and the glycolysis; increasing it from 5 to 20 per cent had no effect on glycolysis but depressed the oxygen uptake from 31 to 19. In mediums containing dextrose and 1 per cent carbon dioxide–bicarbonate buffer the addition of succinate increased the oxygen uptake from 12 to 16 without affecting glycolysis; succinate, however, had no effect on a medium containing dextrose and phosphate.

Shaffer, Chang and Gerard,[74] in studying the influence of blood constituents on tissue metabolism, reported that in dog retina the oxygen consumption was 187 per cent greater in serum than in Ringer's solution; in other tissues this increase is related to serum proteins. Ideta [75] observed the effect of sugar concentration on the metabolism of rabbit retina and found that the respiratory rate increased

69. Elliott, K. A. C., and Baker, Z.: The Effects of Oxidation-Reduction Potential Indicator Dyes on the Metabolism of Tumour and Normal Tissues, Biochem. J. **29**:2396, 1935.

70. Oyama, N.: Einfluss der Wasserstoffionenkonzentration auf den Säuerstoffverbrauch der Hellnetzhaut von Kaninchen in vitro, Tohoku J. Exper. Med. **35**:576, 1939.

71. Oyama, N.: Einfluss des Natriumbikarbonats auf den Säuerstoffverbrauch der Hellnetzhaut von Kaninchen in vitro, Tohoku J. Exper. Med. **37**:78, 1939; abstracted, Chem. Abstr. **34**:2051, 1940.

72. Laser, H.: Metabolism of Retina, Nature, London **136**:184, 1935.

73. Craig, F. N., and Beecher, H. K.: The Effect of Carbon Dioxide Tension on Tissue Metabolism (Retina), J. Gen. Physiol. **26**:473, 1943.

74. Shaffer, M.; Chang, T. H., and Gerard, R. W.: The Influence of Blood Constituents on Oxygen Consumption in Nerve, Am. J. Physiol. **111**:697, 1935.

75. Ideta, K.: Studien über die Gewebsatmung der Netzhaut des Kaninchens in Vitro: Einfluss des Zuckers im Serum, Jap. J. M. Sc., III, Biophysics **5**:105, 1938.

with increasing sugar concentrations up to a maximum at 0.5 per cent, while glycolysis was greatest at a concentration of 0.2 to 0.4 per cent. Oguchi [76] also noted that the metabolism of rabbit retina was greater in serum than in Ringer's solution. Aerobic glycolysis was present in serum, but the Pasteur effect was prominent. In both mediums the temperature coefficient increased slowly with time, this increase, the author stated, indicating tissue damage.

Considerable information on the chemical changes which take place in retinal metabolism has been gained in recent years by groups of investigators who have studied the formation and effect of intermediary products. In 1935 Possenti [77] observed that the aerobic and anaerobic glycolysis of the retina was higher than that of any other normal tissue and was comparable to that of tumor tissue. The production of lactic acid from dextrose was higher than that from hexosediphosphoric acid. From α-glycerophosphoric acid and phosphoglyceric acid, although they were actively metabolized, the lactic acid production was very small and was not influenced by mixing α-glycerophosphoric acid and phosphoglyceric acid or by the addition of pyruvic acid to α-glycerophosphoric acid. Hexosediphosphoric acid, α-glycerophosphoric acid and phosphoglyceric acid showed an induction period for formation of lactic acid, probably due to dephosphorylation. They found no liberation of phosphoric acid from the retina during glycolysis.

Süllmann and Vos [62] asserted that an extract of ox retinas inactivated by dialysis was able to produce lactic acid after the addition of muscle adenylic acid. Cozymase alone could not activate it. Manganese, magnesium and pyruvic acid increased the formation of lactic acid. While dextrose, mannose and fructose were equivalent as substrates, galactose yielded only small amounts of acid. Hexosediphosphate gave much less lactic acid than did dextrose, but dextrose-1-phosphate gave as much. Inorganic phosphate was found necessary for glycolysis. Nicotinic acid, nicotine or nicotinamide had no stimulatory effect on metabolism. When inosinic acid was used instead of adenylic acid, there was no phosphorylation or lactic acid production. In a subsequent study Süllmann [78] found that inosinic acid could function in retinal extracts as a coenzyme in the phosphorylation of both glucose and glycogen, although not as effectively as adenylic acid.

76. Oguchi, T.: Experimentelle Studien über den Einfluss des verschiedenartigen Bedingungen auf den Stoffwechsel der Netzhaut: I. Der physiologische Stoffwechsel der Kaninchennetzhaut in Ringerlösung und im Serum, Acta Soc. ophth. jap. **40**:1568, 1936; abstracted, p. 96.

77. Possenti, G.: Prime ricerche sulla glicolisi retinica, Riv. di pat. sper. **15**:183, 1935.

78. Süllmann, H.: Ueber die CO-Enzymwirkung von Inosinsäure beim Glucose- und Glykogenabbau in Extrakten der Retina, Helvet chim. acta **23**:606, 1940.

Mixtures of the acids were not as effective as adenylic acid alone, but inosinic acid did not inhibit adenylic acid.

Süllmann and Brückner [79] showed that glycolytic extracts of ox retinas break down glycogen chiefly via phosphorolysis. The addition of dextrose-1-phosphoric acid inhibited the phosphorylation of dextrose and of glycogen. In experiments with dextrose plus glycogen, dextrose plus dextrose-1-phosphoric acid and glycogen plus dextrose-1-phosphoric acid there was no additional lactic acid formation. Retinal extracts were able to form glycogen from dextrose-1-phosphoric acid, this reaction being accelerated by muscle adenylic acid. These authors also studied the transformation of dextrose-1-phosphoric acid to hexosediphosphoric acid.

Kerly and Bourne [60] noted that aqueous extracts of ox retina converted dextrose, glycogen or hexosediphosphate into lactic acid on the addition of adenosine triphosphate or adenylic acid. Adding phosphate or magnesium increased formation of lactic acid from dextrose, and the yield of hexosediphosphate was increased by magnesium but not by phosphate. After dialysis of the extract there was no formation of lactic acid from dextrose unless magnesium and phosphate were added; for formation from glycogen only phosphate, and from hexosediphosphate only magnesium, was required. In the experiments adenylic acid could replace adenosine triphosphate but with less yield; with added phosphate, however, there were greater yields of lactic acid with adenylic acid. Cozymase could not replace either adenosine triphosphate or adenylic acid. In extracts incubated with dextrose there was no evidence of phosphoric-carbonic esters. With adenylic acid used as the coenzyme there was a transfer of inorganic phosphate to an ester, probably adenosine triphosphate. With hexosediphosphate as the substrate almost all was broken down to inorganic phosphate. The incubation of dextrose with hexosediphosphate gave only slightly more lactic acid than dextrose alone.

In studying the phosphorylating glycolysis of various tissues, Meyerhof and Perdigon [80] found that the oxidation-reduction process between pyruvic acid and triose phosphate, formed from hexosediphosphate, was rapid in the retina, especially if hexosemenophosphate and creatine were present. The addition of a coenzymatic system, such as cozymase and adenosine triphosphate, increased the speed of glycolysis.

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79. Süllmann, H., and Brückner, R.: Glykogenolyse und Glykogenbildung in Extrakten der Retina, Enzymologia **8**:167, 1940.

80. Meyerhof, O., and Perdigon, E.: Sur la glycolyse phosphorylante des tissus animaux, Enzymologia **8**:353, 1940.

Greig, Munro and Elliott [81] discovered that the oxidation in the retina was different from that in most other tissues studied in that pyruvate did not seem to be removed by the succinate-fumarate-malate-oxalacetate series. Lactate and pyruvate were oxidized rather rapidly. Succinate was oxidized only slightly to fumarate, and there was an equilibrium established between fumarate and malate, but with no further oxidation. Fumarate caused an unexplained lowering of the respiratory quotient. Acetate, formate, β-hydroxybutyrate, citrate and α-ketoglutarate were not oxidized to any extent. This would indicate that oxidation probably does not take place through the Krebs citric acid cycle, although Krause and Stack [82] noted a fairly high citric acid content in the retina, which might suggest this scheme. The manometric work of Greig and associates [81] showed that some acid intermediate other than pyruvate was formed from lacate during the first stage of the experiment and that later, when lactate was no longer oxidized, the unknown acid acted as a substrate.

Possenti [83] found no, or only traces of, carboxylase in the retina and suggested that, instead of carbon dioxide being split from pyruvic acid to yield acetaldehyde, the Törniessen scheme was employed, whereby two pyruvates form a diketo fatty acid, which splits into succinic and formic acids. Meyerhof and Lohmann [84] demonstrated the presence of zymohexase, which splits hexosediphosphate in the retina; and Elliott and Greig,[85] the presence of complete succinic oxidase, indophenol oxidase and succinic dehydrogenase systems in the retina. The oxygen uptake was increased to a maximum through the addition of cytochrome-C.

In the retina, Weil-Malherbe [86] showed that *l*-glutamic acid did not affect anaerobic gycolysis, in contrast to its inhibitory action in the

81. Greig, M. E.; Munro, M. P., and Elliott, K. A. C.: The Metabolism of Lactic and Pyruvic Acids in Normal and Tumour Tissue: VI. Ox Retina and Chick Embryo, Biochem. J. **33**:443, 1939.

82. Krause, A. C., and Stack, A. M.: Citric and Malic Acids of the Ocular Tissues, Arch. Ophth. **22**:66 (July) 1939.

83. Possenti, G.: Ricerche sul ricambio dell'acido piruvico nella retina, Riv. di pat. sper. **15**:229, 1935.

84. Meyerhof, O., and Lohmann, K.: Ueber die enzymatische Gleichgewichtsreaktion zwischen Hexosediphosphorsäure und Dioxyacetonephosphorsäure: III. Ueber Abfangen der Triosephosphorsäure mit Bisulfit und die Verbreitung des Ferments; "Zymohexase," Biochem. Ztschr. **273**:413, 1934.

85. Elliott, K. A. C., and Greig, M. E.: The Distribution of the Succinic Oxidase System in Animal Tissues, Biochem. J. **32**:1407, 1938.

86. Weil-Malherbe, H.: Observations on Tissue Glycolysis, Biochem. J. **32**: 2257, 1938.

brain. Santoni [87] found that glutamic acid increased respiration. Greig and Munro [88] demonstrated that pyrophosphate had practically no effect on the normal respiration of the retina but considerably increased the rate of oxidation of glucose and lactate. By studying frozen-dried sections of the retina, Anfinsen [89] was able to show that the adenosine diphosphate was greater in the synaptic layers and the ganglion cell layer and less in the rods and cones.

In studying the oxidation-reduction systems in the retina, Süllmann and Schmid [90] found the ascorbic acid content to be 15 mg. per hundred grams (determined by titration) and that there was no difference between the light-adapted and the dark-adapted eye. Deproteinized retinal extracts gave a positive nitroprusside reaction, indicating the presence of sulfhydryl groups. Kodamari [91] noticed that the normal light-adapted rabbit retina contained 147.2 mg. of glutathione but that the dark-adapted retina contained 32 per cent less. Bleeding, cyanide, cocaine, ligation of the bile ducts and avitaminosis A, all conditions which decrease dark adaptation, increased the glutathione content of the retina.

Von Euler and Adler [92] noted the high content of flavin (evidently riboflavin) in the retina. Gourévitch [93] expressed the belief that the flavin content of rat retina corresponded in general to the intensity of the residual respiration. Süllmann [94] showed that added lactoflavin caused a loss of pyruvic acid when the mixture was illuminated.

87. Santoni, A.: Ulteriori ricerche sul metabolismo della retina; metabolismo degli aminoacidi, Rassegna ital. d'ottal. **9**:81, 1940; abstracted, Am. J. Ophth. **23**: 1290, 1940.

88. Greig, M. E., and Munro, M. P.: Some Effects of Pyrophosphate on the Metabolism of Tissues, Biochem. J. **33**:143, 1939.

89. Anfinsen, C. B.: The Distribution of Diphosphopyridine Nucleotide in the Bovine Retina, J. Biol. Chem. **152**:279, 1944.

90. Süllmann, H., and Schmid, A. E.: Ueber die Oxydoreduktionssysteme der Netzhaut, Ophthalmologica **103**:150, 1942.

91. Kodamari, S.: Ueber Glutathion in der Netzhaut von Kaninchenaugen: I. Ueber den Gehalt von Glutathion in der Netzhaut bei normalen Kaninchen und einige daran anschliessende Experimente, Acta Soc. ophth. jap. **39**:2053, 1935; abstracted, p. 147; II. Ueber den Gehalt von Glutathion in der Netzhaut und einiger anderer Organe bei Kaninchen unter verschiedenen Bedingungen, ibid. **40**: 2444, 1936; abstracted, p. 159.

92. von Euler, H., and Adler, E.: Ueber das Vorkommen von Flavinen in tierischen Geweben, Ztschr. f. physiol. Chem. **223**:105, 1934.

93. Gourévitch, A.: La distribution de la flavine dans les tissus des mammifères, en relation avec leur respiration résiduelle en présence des cyanures, Compt. rend. Acad. d. sc. **204**:526, 1937.

94. Süllmann, H.: Sensibilisierende Wirkung des Lactoflavins bei der photochemischen Umwandlung von Brenztraubensäure, Klin. Wchnschr. **7**:1157, 1938.

Theorell [95] asserted that the destruction of flavin or its ester proceeds more rapidly in the presence of oxygen and more rapidly in alkaline than in neutral mediums. Stern, Melnick and DuBois [96] studied the nature of Pasteur enzyme in the retina and showed it to be a pheohemin protein, similar to the respiratory enzyme in yeast and in Acetobacter but differing in its affinity for carbon monoxide and oxygen and in its absorption spectrum.

Respiratory Quotient.—Dickens and Simer,[97] together with other investigators, concluded that the respiratory quotient of the retina was 1 and thus placed retina in the group of tissues, including brain, chorion and embryo, in which the metabolism consists strictly in the oxidation of carbohydrates. This view has been recently opposed by Elliott and Baker,[98] who obtained a value of 0.91 for rat retina and of 0.86 for rat brain. Possenti [83] obtained a respiratory quotient of 0.8 to 0.9 in Ringer's solution, which became over 1.0 when pyruvate was added.

Fat Metabolism.—An explanation for a respiratory quotient below 1.0 may be given by recent work, which suggests the part played by a fat metabolism. Sgrosso [99] found in ox retina high quantities of a lipase for the low neutral fats but not for the high neutral fats. Santoni [100] showed that ox or rabbit retina oxidized numerous fatty acids, with the exception of formic, caproic and oleic acid. These acids inhibited the respiration. It was found that the methyl esters of the fats had a greater capacity for oxidation than the free fats. He suggested that these esters may be those normally found in the cells rather than the esters produced by the action of enzymes.

Formation of Ammonia.—Warburg, Posener and Negelein [28] noticed that large quantities of ammonia were formed during anaerobic glycolysis in the retina and brain, and even larger quantities during aerobic

95. Theorell, H.: Quantitative Bestrahlungsversuche an gelbem Ferment, Flavinphosphorsäure und Lactoflavin, Biochem. Ztschr. **279**:186, 1935.

96. Stern, K. G.; Melnick, J. L., and DuBois, D.: Nature of the Pasteur Enzyme, Science **91**:436, 1940. Stern, K. G., and Melnick, J. L.: The Photochemical Spectrum of the Pasteur Enzyme in Retina, J. Biol. Chem. **139**:301, 1941.

97. Dickens, F., and Simer, F.: The Metabolism of Normal and Tumour Tissue: II. The Respiratory Quotient, and the Relationship of Respiration to Glycolysis, Biochem. J. **24**:1301, 1930.

98. Elliott, K. A. C., and Baker, Z.: The Respiratory Quotients of Normal and Tumour Tissue, Biochem. J. **29**:2433, 1935.

99. Sgrosso, S.: Ricerche sui fermenti lipolitici della retina, Rinasc. med. **11**: 334, 1934.

100. Santoni, A.: Sulla capacità del tessuto retinico di ossidare alcuni acidi grassi ed esteri metilici di acidi grassi "in vitro," Ann. di ottal. e clin. ocul. **67**:845, 1939; abstracted, Am. J. Ophth. **23**:729, 1940.

glycolysis. Rösch and te Kamp [101] found that retina gave off over 50 per cent of ammonia from muscle adenosine-5-phosphoric acid, 20 per cent from yeast adenosine-3-phosphoric acid, some from adenosine but none from adenine. Light-adapted retina gave 5.22 mg., and dark-adapted retina 0.74 mg., of ammonia per hundred grams. Lighting the dark-adapted retina increases the ammonia content at least 72 per cent. Stutzke [102] obtained increases of 200 to 500 per cent in ammonia content on illuminating the dark-adapted retina but no increase in the light-adapted retina. Dextrose lactate or pyruvate inhibited this evolution of ammonia. Rösch [103] observed that visible light and roentgen rays of long medium wavelength, but not ultraviolet rays, caused the evolution of ammonia, in proportion to the intensity of light. Dickens and Greville [104] found production of ammonia to be small in the retina, but in the absence of dextrose or fructose it became large relative to the respiratory rate, partly because of the large fall in the latter.

Glycogen.—The presence of glycogen in the retina has been a subject of some dispute. Ehrlich,[105] in 1833, detected glycogen in frog retina, and Luna,[106] Müller [107] and others found it in other animals. Best [108] and Matsuoka [109] claimed that the normal retina was free of glycogen, but Schmitz-Moormann,[110] with careful staining, demonstrated glycogen in the inner segment in the base of the cones and in the myoid

101. Rösch, H., and te Kamp, W.: Ueber Ammoniakbildung bei Belichtung der Netzhaut, Ztschr. f. physiol. Chem. **175**:158, 1928.

102. Stutzke, S.: Ueber die Ammoniakbildung in der Netzhaut, Klin. Wchnschr. **15**:524, 1936.

103. Rösch, H.: Weitere Untersuchungen über die Ammoniakbildung in der Netzhaut, Ztschr. f. physiol. Chem. **186**:237, 1930.

104. Dickens, F., and Greville, G. D.: The Metabolism of Normal and Tumor Tissue: IX. Ammonia and Urea Formation, Biochem. J. **27**:1123, 1933.

105. Ehrlich, P.: Ueber das Vorkommen von Glykogen im diabetischen und im normalen Organismus, in Frerich, F. T.: Ueber den plötzlichen Tod und über das Coma bei Diabetes, Ztschr. f. klin. Med. **6**:3, 1833.

106. Luna, E.: Ricerchi istologische e istochimiche sulla retina dei vertebrati, Monitore zool. ital. **22**:119, 1911.

107. Müller, C.: Das Glycogen der Retina des Frosches, Ztschr. f. d. ges. Anat. **81**:220, 1926.

108. Best, F.: Demonstration mikroskopischer Präparate vom diabetischen Auge, Ber. ü. d. Versamml. d. deutsch. ophth. Gesellsch. **32**:315, 1906; Die Bedeutung des pathologischen Glykogengehaltes, Zentralbl. f. allg. Path. u. path. Anat. **18**:465, 1907.

109. Matsuoka, J.: Ueber das Glykogen in der Netzhaut, Nippon Gankwa Gakkawi Zasshi **23**:1919; cited by Schmitz-Moormann.[110]

110. Schmitz-Moormann, P.: Ueber der Glykogengehalt der Retina und seine Beziehungen zur Zapfenkontraktion, Arch. f. Ophth. **118**:506, 1927.

but not in the rods. Fontana [111] saw glycogen granules in the pigment epithelium, in the cones and in the external limiting membrane. There was no glycogen in the pigment epithelium if the eyes were kept in the dark, but much in bright light; the other deposits of glycogen remained unchanged. Brammertz,[112] on the other hand, detected in the eye of the housefly an increase of glycogen in the dark-adapted eye and a decrease in the light-adapted eye.

Best [113] found that ocular inflammations, subconjunctival injections of a 10 per cent solution of sodium chloride, subcutaneous injections of phlorhizin and diabetes increased the retinal glycogen. Majima [6] and Nakayasu [114] noted that epinephrine increased the glycogen. Nakayasu also found that the injection of 10 units of insulin per kilogram produced a fall or disappearance of glycogen in the retina, 5 units a slight reduction and ½ unit a rise. Thyroxin or thyroid extract produced a rise of glycogen, as also did solution of posterior pituitary U. S. P. Trematori [115] investigated the amylase of the retina and found it to have an optimum of p_H of 7.8 and an optimum sodium chloride concentration of 0.008 to 0.013 per cent. Fluoride completely inhibited, and hydrogen peroxide and formaldehyde partially inhibited, the amylase.

Carbon Dioxide Anhydrase.—Bakker [116] found a high concentration of this enzyme in the retina and lens, some in the cornea and choroid and none in the sclera. He assumed that tissues with a high aerobic glycolysis and a paucity of blood vessels need a high concentration to catalyze the rapid dissolution of carbon dioxide. He [117] showed that carbon dioxide anhydrase produced both a hydration and a dehydration of carbon dioxide, although in the retina dehydration occurs more readily than hydration. The reaction was activated in both directions by cysteine, histidine, histamine and glutathione.

111. Fontana, G.: Ulteriori ricerche istologische sul glicogeno della retina di alcuni vertebrati allo stato normale ed in talune condizioni sperimentali, Rassegna ital. d'ottal. **4**:135, 1935.

112. Brammertz, W.: Ueber das normale Vorkommen von Glykogen in der Retina, Arch. f. mikr. Anat. **86**:1, 1914.

113. Best, F.: Beitrag zur Wirkung subconjunctival Injektionen, Arch. f. Augenh. **57**:173, 1907; footnote 108.

114. Nakayasu, S.: Ueber den Einfluss der verschiedenen Präparate der inneren sekretorischen Organe auf den Glykogenstoffwechsel in der Netzhaut, Acta Soc. ophth. jap. **37**:941, 1933; abstracted, p. 71.

115. Trematori, M.: L'amilasi della retina, Riv. biol. **20**:108, 1936.

116. Bakker, A.: Der Kohlensäureanhydrasegehalt verschiedener Augengewebe einiger Säugetiere, Ophthalmologica **102**:351, 1941.

117. Bakker, A.: Bewirkt die Kohlensäureanhydrase in den Augengeweben eine Hydratation von Kohlendioxyd oder eine Dehydratation von Kohlensäure? Ophthalmologica **103**:88, 1942.

Acetylcholine.—Lange [118] found that after dark adaptation 20 frog retinas (0.5 Gm.) contained 150 micrograms of acetylcholine, while after light adaptation the same number contained only 15 micrograms. Similar results on the effect of light were obtained by Chang, Hsieh, Lee and Li; [119] Nakashima and Murata,[120] and Chang, Lee and Li.[121] Bakker [122] demonstrated the formation of acetylcholine in the retina by noticing the action of an explanted iris when the retina was also explanted. Anfinsen [123] demonstrated that cholinesterase occurred chiefly in the synaptic layers of the retina.

Detached Retina.—By studying the special metabolism of the detached retina, some clues may be obtained as to normal retinal metabolism. Weve and Fischer [124] showed that, while normal retina in contact with the pigment epithelium has a low oxidation-reduction potential, the detached retina was more highly oxidized, this oxidation being evidently due to an alteration in its metabolism. On detachment it was no longer glycolysis, but respiration, which prevailed. Glycolysis and vision seemed to depend on the contact of retina with pigment epithelium. Fischer [125] showed the detached retina to be more acid. Weve and Fischer [126] demonstrated a high amylase content of the subretinal fluid, liberated as a result of autolysis of retinal cells and not due to any admixture of blood. Amylase was found to occur

118. Lange, V.: Ueber das Vorkommen von Azetylcholin im hell- und dunkeladaptierten Auge, Ztschr. f. physiol. Chem. **279**:73, 1943; abstracted, Chem. Abstr. **38**:3024, 1944.

119. Chang, H.; Hsieh, W. M.; Lee, L. Y., and Li, T. H.: Diminution of Acetylcholine Content of Retina After Prolonged Functional Disuse, Proc. Soc. Exper. Biol. & Med. **43**:140, 1940.

120. Nakashima, M., and Murata, G.: Ueber die Cholinmenge der Hell- und Dunkelnetzhaut, Acta Soc. ophth. jap. **43**:660, 1939; abstracted, p. 41.

121. Chang, H. C.; Lee, L. Y., and Li, T. H.: Tissue Acetylcholine: IX. Diminution of Acetylcholine of Retina During Functional Disuse, Chinese J. Physiol. **16**:373, 1941.

122. Bakker, A.: Ueber Acetylcholinbildung in der Retina, Arch. f. Ophth. **141**:326, 1939; abstracted, Chem. Abstr. **34**:3801, 1940.

123. Anfinsen, C. B.: The Distribution of Cholinesterase in the Bovine Retina, J. Biol. Chem. **152**:267, 1944.

124. Weve, H. J. M., and Fischer, F. P.: Le métabolisme de la rétine décollée, Ann. d'ocul. **175**:817, 1938.

125. Fischer, F. P.: Metabolismus der abgelösten Netzhaut, Nederl. tijdschr. v. geneesk. **83**:4187, 1939; abstracted, Zentralbl. f. d. ges. Ophth. **44**:395, 1939.

126. Weve, H. J. M., and Fischer, F. P.: Ueber die Amylase der subretinalen Flüssigkeit, Arch. f. Augenh. **110**:390, 1937.

only in the retina.[127] A high acetylcholine esterase content was observed in subretinal fluid.[128]

COMMENT

The foregoing evidence is not sufficient to allow one to outline an integrated framework of retinal metabolism; yet one may list, without attempting to connect, some of the important reactions in accordance with the weight of the evidence, as few facts stand completely unopposed.

On stimulation with light, acetylcholine is liberated in the retina, this perhaps being the substance which stimulates the nerve elements; phosphocreatine is converted into creatine and phosphoric acid, and adenosine triphosphate is split into the disphosphate and phosphoric acid, in addition to the fundamental conversion of rhodopsin into other products. The decomposition of phosphocreatine and adenosine triphosphate results in the liberation of energy, possibly both reactions occurring in a stepwise fashion. The energy, then, for the reformation of rhodopsin, phosphocreatine, adenosine triphosphate and perhaps other substances, as well as the basal energy requirements of the cells, comes largely from the oxidation of glucose. The effect of poisons and substrates and of added enzyme systems and the determination of intermediate products would indicate that glycolysis follows a scheme similar to that of muscle: glucose through the hexosemonophosphates to hexosediphosphate, thence to dioxyacetone phosphate and glyceraldehyde phosphate followed by oxidization to phosphoglycerate and then pyruvate, which yields lactate and is eventually oxidized to carbon dioxide and water. The intermediate substances are not all known, but it may be supposed that the entire Cori scheme is reproduced, and it seems likely that the Krebs citric acid cycle is employed. The Pasteur effect is present. Glycogen, which is probably stored in the normal retina, may supplement blood glucose. Certainly the metabolism, primarily glycolytic, may also involve the oxidation of fats and amino acids, with resulting respiratory quotients below 1.

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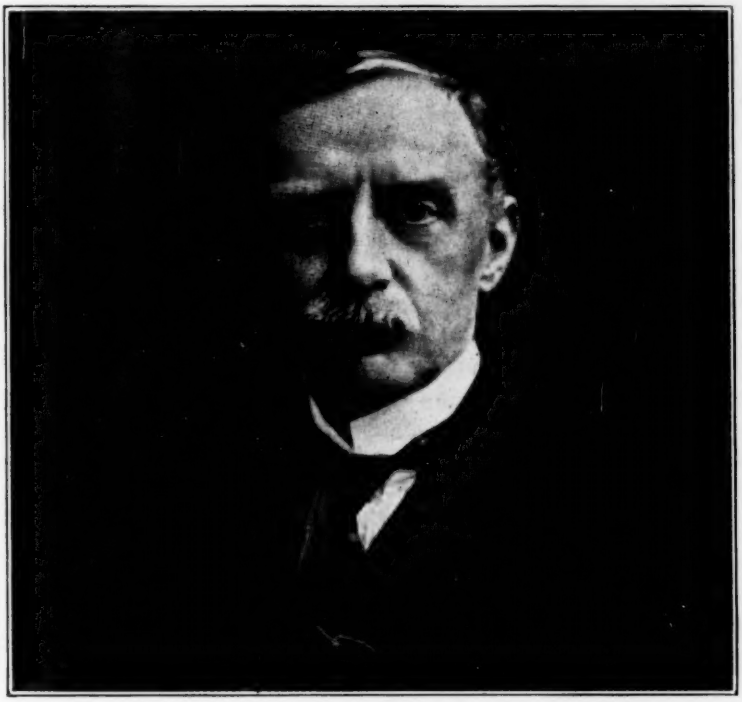
127. Weve, H. J. M.: Der Enzymgehalt der retroretinalen Flüssigkeit, Nederl. tijdschr. v. geneesk. **81**:3000, 1937; abstracted, Zentralbl. f. d. ges. Ophth. **39**:367, 1937.

128. Weve, H. J. M., and Fischer, F. P.: Ueber den Azetylcholinesterase-Gehalt der subretinalen Flüssigkeit bei rupturellen Netzhautablösungen, Ophthalmologica **96**:348, 1939.

Obituaries

ANDREW MAITLAND RAMSAY, M.D.
1859-1946

Dr. Maitland Ramsay died at his home in St. Andrews, Scotland, on March 20, at the age of 86. After receiving his medical education at the University of Glasgow and at the Western Infirmary, he entered general practice and was particularly active in the Charlotte Street Dispensary of the Glasgow Eye Infirmary. In 1898 he was appointed surgeon to the Ophthalmic Institution, which was the eye department



ANDREW MAITLAND RAMSAY, M.D.
1859-1946

of the Glasgow Royal Infirmary, an institution founded by J. R. Wolfe, whose name is known in connection with skin grafting. Dr. Ramsay was instrumental in the foundation of a chair in ophthalmology in the University of Glasgow with a bequest given by L. Gavin Tennent, his friend and teacher, whose bequest also included the construction of the Tennent Memorial Eye Institute.

Dr. Ramsay wrote a number of important books, such as: "Atlas of External Diseases of the Eye," 1898; "Eye Injuries and Their Treatment," 1907; "Diathesis and Ocular Diseases," 1909; "Clinical Ophthalmology for the General Practitioner," 1920, and "The Eye in General Medicine," 1929. The titles of these books show that Dr. Ramsay approached his subject from the standpoint of general medicine. He took every opportunity of encouraging the use of the ophthalmoscope by the internist in the routine examination of his patients and always stressed the close association of ocular disorders and general diseases. Dr. Ramsay was fundamentally a clinical ophthalmologist, following in the tradition of his great predecessor, William Mackenzie. His interest in general medicine remained throughout his life, and he was convinced that the physician's chief duty lay in clinical observation, rather than in dependence on laboratory investigations.

In 1904 Dr. Ramsay attended the annual meeting of the American Medical Association and delivered an address on "The Importance of General Therapeutics in the Treatment of Ocular Diseases."

He retired at the age of 60 and settled at St. Andrews, where, with his wife, who was Dr. Elizabeth Margaret Pace, he lived many happy years and gave much pleasure to those who were fortunate enough to enjoy his hospitality. At the same time he continued his interest in medicine, particularly the investigations that were being carried out in the institution founded by Dr. James Mackenzie.

Tall, of distinguished appearance and gentle manners, Dr. Ramsay endeared himself to patients and colleagues alike. He had firm convictions and views, which he did not hesitate to express, and he was much distressed with the trend of modern medicine. In his last address, "The Making of the Family Doctor," dedicated to the medical students of St. Andrews University, he concluded with the statement that the state can never replace the relationship between the physician and his patient and insisted that it is not possible to buy research on a large scale.

ARNOLD KNAPP.

Abstracts from Current Literature

EDITED BY DR. WILLIAM ZENTMAYER

Anatomy and Embryology

SIMILARITY OF THE DEVELOPING RETINA AND BRAIN WALL IN HUMAN EMBRYOS. H. C. HADEN, Am. J. Ophth. **28:** 943 (Sept.) 1945.

Haden explains the embryonic similarity of the retina and the wall of the brain by means of eighteen illustrations of sections from human embryos.

W. S. REESE.

Aqueous Humor

ROENTGENOLOGIC STUDY OF OUTFLOW OF THE AQUEOUS. M. BALTIN, Vestnik oftal. **24:** 14, 1945.

The basis for this study was the introduction into the anterior chamber of contrasting substances and the follow-up observation on the paths of their outflow in the roentgenograms.

Baltin tried injection of iodized poppyseed oil, sergosin and solution of 20 per cent potassium iodide in rabbit eyes, but none of these substances could be traced. He then used Thorotrast (a colloidal solution of thorium dioxide). After emptying the anterior chamber, 0.1 or 0.2 cc. of the substance was introduced with the same needle. A roentgenologic examination was made every half-hour on the day of the injection and then daily during the time of the observation. The dye could be followed up to the suprachoroidal space. The rabbit eyes were enucleated at various intervals. Histologic examination on the second day showed the presence of round cells in the angle of the anterior chamber, in Fontana's spaces, in the ligamentum pectinatum and in the ciliary body; there were a large number of cells also at the pupillary margin of the iris. Schlemm's canal was free from the cells. These cells contained the thorium dioxide.

Thorotrast was introduced into eyes in which atropine and physostigmine were instilled, as well as into glaucomatous eyes. Roentgenologic examination showed no change in any of these eyes as compared with the normal.

Baltin summed up his experimental work as follows:

1. Roentgenologic examination of 40 rabbit eyes showed the gradual absorption of the dye and its passage from the angle of the anterior chamber ino the suprachoroidal space. Dye was also present on the iris but not in Schlemm's canal; the last factor may lead one to believe that the outflow of the aqueous is accomplished not by filtration but by more complex processes, which are not known at present.

2. The cells which absorb the thorium dioxide belong to the group of macrophages and are called histiocytes. They absorb various colloidal substances introduced into the organism.

3. The roentgenologic method makes it possible to follow in the living eye the passage of substances introduced from outside into the eye. However, since the conditions are not similar to those under normal physiologic conditions, it is not the best way.

O. SITCHEVSKA.

Blind

FUNCTIONAL BLINDNESS IN WARTIME (DIAGNOSIS AND TREATMENT). Z. KOPUL-LEVINA and O. SHERSHEWSKAYA, Vestnik oftal. **23:** 31, 1944.

The case histories of 8 patients with functional blindness are reported.

A private aged 43 lost vision as a result of contusion of the brain and simultaneous trauma of the face with shrapnel. There was also loss of hearing and speech. The patient was stuporous. The diagnosis of functional blindness was established by the presence of analgesia of the lids and normal media and fundi. Psychotherapy as well as hypnosis gradually brought back the vision and hearing and, as a result, improvement in the tone of the central nervous system and return to normal life after four months of hospitalization.

A private aged 48 received a contusion by air waves in the explosion of an aviation bomb. He was unconscious for four hours, after which there were vomiting, nausea, severe headache and loss of hearing, speech, vision and motion. Speech and hearing in the left ear were restored shortly after the contusion, but general asthenia, blindness and loss of hearing in the right ear remained stationary. There was an area of analgesia of the lids and orbit in the shape of spectacle lenses. The media and fundi were normal. The behavior of the patient was of the reactive depressive type. Hypnosis and psychotherapy were instituted; after the first treatment vision was 0.1 in each eye, and within four weeks it was 0.7 in the right eye and 0.8 in the left eye. The general condition improved also.

In 2 privates, aged 30 and 20, respectively, there was concentric contraction of the visual fields after contusion; in the younger patient there were also deaf-mutism and incontinence of the urine. Partial analgesia of the lids was present in both cases. Psychotherapy aided in the restoration of the visual fields to normal.

The diagnosis of functional blindness was made because of analgesia of the region of the lids in the shape of spectacle lenses. Hypnosis and psychotherapy usually give good results.

O. SITCHEVSKA.

Conjunctiva

CHRONIC CONJUNCTIVITIS OF THE INTERNAL ANGLE CONSEQUENT TO IGNORED CANALICULAR MYCOSIS. A. VÁZQUEZ BARRIÈRE and R. V. TALICE, Arch. de oftal. de Buenos Aires **19:** 1 (Jan.) 1944.

Chronic conjunctivitis involving the bulbar conjunctiva in the region of the internal angle which does not respond to treatment may be produced by unsuspected mycosis of the lacrimal canaliculi.

A case is reported in which such a condition occurred. On careful examination it was found that a zone of congestion surrounded the upper punctum, which was open and dilated. Yellow concretions were extracted from the canaliculus, which when examined microscopically showed the presence of the myceliums of Actinomyces.

H. F. CARRASQUILLO.

A GRAVE TYPE OF PURULENT CONJUNCTIVITIS OF THE NEWBORN. A. VILACORO, Arch. Soc. oftal. hispano-am. **4:** 18 (Jan.-Feb.) 1944.

The disease makes its appearance three or four days after birth, with moderate conjunctival congestion. In three days purulent conjunctivitis sets in, with intense congestion of the bulbar and palpebral conjunctiva and abundant discharge over the lids. Two or three days later the inflammation reaches its maximum, and the chemotic conjunctiva shows over the margins of the lids, which are red and swollen. At this time superficial infiltration of the cornea is observed. Ultimately, the entire thickness of the cornea is involved. Perforation may take place. When the condition subsides, the cornea remains opaque, and vision is greatly limited or altogether lost.

All efforts to find the causative agent of the disease have failed. No bacteria or inclusion bodies have been identified. It is thought that some filtrable virus may be responsible.

Treatment is of no avail. The disease lasts two or three months. The author reports 4 cases. Complete blindness resulted in 2 of the cases and partial blindness in the other 2 cases.

H. F. CARRASQUILLO.

Congenital Anomalies

DERMAL LIPOMA OF THE CONJUNCTIVA WITH SCLERAL CYST AND COLOBOMA OF THE PALPEBRAL ANGLE. W. B. MATTOS, Arq. brasil. de oftal. **5:** 39 (April) 1942.

The author presents a clinical observation on a patient 7 years of age. Examination showed a greatly widened palpebral fissure, due to a coloboma of the external angle. In the latter region a large, yellowish rose tumor covered more than half the cornea and extended into the outer portion of the upper and lower cul-de-sacs, preventing the patient from closing the eye. The eye was turned inward, and its movements were much reduced.

Operation was performed, with subconjunctival ablation of the tumor. The conjunctiva was spared as much as possible, the tumor being disinserted from the cornea, to which it was closely adherent. The tumor was dissected along its whole length between the superior, internal and inferior rectus muscles. In the region of the inferior rectus, a scleral cyst was found at 5 o'clock, just behind the limbus. This was not removed but was left for a future operation. As strabismus was present, tenotomy of the internal rectus muscle was performed. At a second operation the scleral cyst was removed and the palpebral coloboma closed. A slight convergent strabismus and a leukoma over one-half the cornea remained.

The author was unable to find any reference in the literature on epibulbar tumors associated with scleral cyst. M. E. ALVARO.

CONGENITAL ANIRIDIA: REPORT OF A CASE. H. MARBACK, Arq. brasil. de oftal. **5:** 97 (June) 1942.

The author presents a case history.

A man aged 20, with no family history of any ocular defect, showed horizontal nystagmus, which increased involuntarily in a strong light

or when the patient tried to fixate objects in distant or near vision. There was complete absence of the iris in both eyes, resulting in an excessively large pupillary orifice, the limit of which was determined by the contour of the cornea, which was of normal size. The cornea was transparent, except in the lower limbal region, where there was a partial embryotoxon. The lens was semidislocated and rotated upward and backward, completely opacified and of a grayish white color. The fundus was normal. In each eye visual acuity taken with a + 13 D sphere was limited to counting fingers at 3 meters. This acuity was relatively good for a case of this kind and in accord with the normal aspect of the fundus, as in the great majority of cases aniridia is associated with absence of the macula.

The author agrees with Duke-Elder that two different mechanisms may produce the same anomaly, 1. Aniridia may result from lack of development of the retinal ectoderm at the level of the edge of the optic vesicle. That aniridia is always associated with other ectodermal defects supports this theory. 2. The anomaly may be the result of a malformation of the vascular mesoderm, due to a mechanical obstruction in the development of the iris, caused by remnants of the fibrovascular capsule of the lens.

M. E. ALVARO.

Experimental Pathology

PIGMENTARY MOBILIZATION PROVOKED BY LESION OF THE CERVICAL SYMPATHETIC GANGLION. R. RODRIGUEZ BARRIOS, Arch. de oftal. de Buenos Aires **18:** 709 (Dec.) 1943.

In the course of a series of experiments to ascertain the action of the sympathetic nervous system on the eye, Rodriguez Barrios observed the following phenomenon: A few days after extirpation of the superior cervical ganglion, mobilization of pigmentary cells (melanophores) was observed. Invasion of the periphery of the cornea by these cells appeared four days later and progressed, forming an annular zone, which reached a width of 2 mm. in some places.

The observation is reported in the hope that further experiments will be carried out on this line of investigation.

H. F. CARRASQUILLO.

General Diseases

MARFAN'S SYNDROME. C. H. JOLLY and O. H. SOLA, Arch. de oftal. de Buenos Aires **18:** 697 (Dec.) 1943.

The authors report a clinical case of the disease in a boy aged 14, who was 185 meters (72½ inches) tall and weighed only 60 Kg. (130½ pounds). Exaggerated height and obesity occurred in his ancestors.

The abnormal length of his hands and feet was conspicuous. Clinical and roentgenographic examinations of his hands showed arachnodactyly. There was no abnormality of the heart. Ocular examination demonstrated the presence of bilateral ectopia of the crystalline lens. With corrections of + 4.00 D. sph. for the right eye and a + 7.00 D. sph. for the left eye vision was 1/2 to 1/10 in the respective eyes.

H. F. CARRASQUILLO.

OPHTHALMOPATHIES OF TUBERCULOUS ORIGIN. P. FILHO, Arq. brasil. de oftal. **5:** 101 (June) 1944.

The author first discusses syphilis and focal infections, pointing out that these disease processes cause lesions similar to those of tuberculosis and that, instead of one's being so ready to make a diagnosis of syphilis, tuberculosis should be considered more often.

Patients with ocular tuberculosis often show no general symptoms, tuberculosis rarely being apparent in other parts of the body. The various tests for the diagnosis of tuberculosis are discussed, their value being doubtful, as a low degree of sensitivity to tuberculin and lack of other clinical signs are noted sometimes in patients with old tuberculosis. Torpid uveitis, especially that occurring after operation, is discussed, and 2 cases of the latter type are reported. Sympathetic ophthalmia and Boeck's sarcoid are also discussed. M. E. ALVARO.

Glaucoma

LATE RESULTS OF CYCLODIALYSIS FOR GLAUCOMA. N. IVANOV, Vestnik oftal. **24:** 66, 1945.

Cyclodialysis was suggested by Heine in 1905 for relief of chronic glaucoma as a means of establishing a connection between the anterior chamber and the suprachoroidal space.

The results of cyclodialysis were observed in 100 patients. The period of observation was from two to five years for 87 patients and from five to eight years for 13 patients. The tension, visual acuity and visual fields were tested periodically in the Moscow University Eye Clinic. Fifty-one patients had chronic inflammatory glaucoma, 45 simple glaucoma and 4 secondary glaucoma.

A detailed analysis of the cases is given. Ivanov believes that cyclodialysis is a safe operation, with no complications as a rule; the earlier it is done, the better is the chance of obtaining improved vision, visual fields and tension. His conclusions are as follows:

1. Cyclodialysis was performed on 100 patients with glaucoma, the time of observation being from two to eight years. Intraocular tension became normal in 70.6 per cent of patients with chronic inflammatory glaucoma and in 51.1 per cent of patients with simple glaucoma.

2. The visual acuity remained unchanged in 39.2 per cent of patients with chronic inflammatory glaucoma and in 17.7 per cent of patients with simple glaucoma. In 26 per cent of patients blindness followed, and in 18 per cent cataract developed.

3. Cataract develops in hypotonic eyes as a result of postoperative changes in the ciliary body.

4. The visual fields remained unchanged in 60.8 per cent of patients with chronic inflammatory and in 31 per cent of patients with simple glaucoma.

5. Myopia developed in 11 per cent of emmetropic and hyperopic eyes and increased in 3 per cent of myopic eyes. O. SITCHEVSKA.

Injuries

CHOLINESTERASE CONTENT OF THE EYE. R. Brückner, Ophthalmologica **105:** 37-49 (Jan.) 1943.

Brückner presents investigations on the presence and importance of cholinesterase in the eye, particularly in the aqueous humor and the vitreous body. Studies on horses and cows revealed that cholinesterase is a regular constituent of the aqueous humor, and it is assumed that this is the case also in man. The esterase found in the aqueous probably is derived not from the blood but from other sources. The esterase values of the vitreous body of cows, calves and hogs were several times as high as those of the aqueous humor; in cows it was four times as high as in the serum; in horses the esterase values of the vitreous body were occasionally lower than those of the aqueous. In cows the concentration of esterase varied in the different parts of the vitreous; it was greatest in the peripheral zones. The esterase of the vitreous body is probably derived chiefly from the retina.

J. A. M. A. (W. ZENTMAYER)

TREATMENT OF WAR BLINDNESS. P. TIKHOMIROV, Vestnik oftal. **28:** 10, 1944.

Blindness in wartime is due chiefly to perforating injuries of both eyes, which are severer than injuries in peacetime. They consist of injury to the cornea and sclera, prolapse of the iris, traumatic cataract and large tears in the choroid and retina. Contusions are the second most frequent cause of blindness. Frequently the blindness in one eye was due to a perforating injury and in the second to blunt trauma. According to the statistics of several military hospitals, bilateral injury of the eyes is met with in 15 per cent of all cases of ocular injuries. Tikhomirov divides into four types the complications resulting from injuries in which treatment may restore vision, namely, traumatic cataract, opacities of the cornea, detachment of the retina and hemophthalmos.

His first group consisted of cases of injury to the lens. In 67 per cent traumatic cataract was observed in the only remaining eye (the second eye was enucleated), and in 33 per cent of cases the second eye was normal. Only in 17 per cent of cases was there no complication. In 83 per cent the following complications occurred: foreign bodies, both magnetic and nonmagnetic, in the episclera, the cornea, the ciliary body and the posterior part of the eye; posterior synechia, and corneal opacities. When the cataract became tumescent and caused glaucoma, a linear extraction of the lens normalized the tension. As a rule extraction of the cataract was done within one to two months of the injury, but when there was but one eye the operation was done after all danger of infection from the conjunctiva, the tear sac and foci of infection was eliminated. In some cases immediately after the extraction the magnet was used for removal of the intraocular foreign body. In some eyes the foreign body (at times multiple) could be seen in the eye long after the extraction was done, but the eyes remained quiet over long periods of observation. Cataract formed always as the result of perforating trauma of the eye.

The second group consisted of cases of corneal opacities, frequently the result of injury by mines. Total leukomas with anterior and posterior synechias often were complicated with secondary glaucoma. A number of operations for glaucoma must be performed at times in order to stabilize the tension. The most effective proved to be Vogt's method—diathermy coagulation of the ciliary body. In 10 eyes a corneal transplantation was done, and in 1 eye with dense opacities keratoplasty was done five times before any vision was obtained.

The third group consisted of cases of retinal detachment—those in which the lesion was caused by retinitis proliferans and the prognosis was usually poor and those in which a tear was found. In these cases diathermy was usually successful. A military physician had received bilateral perforating injuries of the eyes with glass. After five operations for traumatic cataract total retinal detachment developed in the right eye and a partial detachment in the left eye. Two operations resulted in restoration of ability to count fingers in the left eye only.

The fourth group consisted of cases of intraocular hemorrhage. Hemorrhage into the eye is frequently the cause of blindness in cases of ocular injuries because the blood organizes and produces retinitis proliferans and retinal detachment. With conservative treatment the hemorrhages may absorb within five to six months. The treatment should be started early with evacuation of the blood.

Thus, Tikhomirov believes that the treatment of blindness due to war injuries results in improvement of vision. The methods may vary, but persistence on the part of physician and patient and a number of operations may restore at least partial vision.

O. SITCHEVSKA.

Instruments

THE STANDARDIZATION OF SO-CALLED SCHIØTZ TONOMETERS. P. C. KRONFELD, Am. J. Ophth. **28:** 34 (Jan.) 1945.

Kronfeld discusses standardization of tonometers and concludes that the method of standardization by measuring the physical properties is sound.

W. S. REESE.

NEW PERMANENT HAND MAGNET IN THE LIGHT OF PRESENT DAY MAGNET-OPERATION METHODS. B. S. BRODSKY, Am. J. Ophth. **28:** 1245 (Nov.) 1945.

Because of the inconvenience of the giant magnet, Brodsky devised a permanent magnet made of iron, nickel and aluminum and the alloy Alnico. He describes his method in cases in which a magnet was used in extraction.

W. S. REESE.

Methods of Examination

FALT'S TEST FOR ESTABLISHING UNILATERAL BLINDNESS, MARKED DECREASE OF VISION OR MALINGERING. M. M. BALTIN, Vestnik oftal. **23:** 22, 1944.

The test is made as follows: The subject is asked to fix the approaching finger or light at 15 cm. As the finger comes closer, the

blind or poorly seeing eye starts to diverge; if both eyes see, normal convergence will be maintained. With this test a unilateral paralysis of accommodation can also be established.

Baltin has used this test for many years and confirms Falt's claims for its usefulness. The test is simple and needs no instruments; it does not depend on the intelligence of the subject; it aids in determining not only unilateral blindness but pronounced reduction of vision. Malingering is fully established. If the test gives a positive result, it is usually impossible to correct the vision. It can be demonstrated to outside observers.

O. SITCHEVSKA.

Neurology

OCULAR NEUROVEGETATIVE SYSTEM: BLUE EYES AND BROWN EYES. F. VIDAL and C. S. DAMEL, Arch. de oftal. de Buenos Aires **18:** 593 (Nov.) 1943.

Studies made on the neurovegetative system of the eye have proved that in man the sympatheticomimetic drugs act better and in lesser concentration in subjects with light-colored irises.

The author made observations on 200 persons with minor refractive errors, of both sexes and of ages ranging from 5 to 64 years and having apparently normal neurovegetative systems. One patient with heterochromia was included. Fourteen of the subjects tested showed neurovegetative dystonia.

The drugs used were 1 per cent phenylisopropylamine sulfate and 5 per cent *l*-α-phenyl-β-2-methylaminopropanol sulfate. The same number of drops were instilled in the upper limbus in each subject. The experiments showed clearly that sympatheticomimetic drugs act better and in weaker concentrations in persons with light-colored eyes.

The action is greatest in eyes with blue irises and next in eyes with greenish, greenish brown and brown irises, in that order. In the dark brown eyes the effect is slight. In the patient with heterochromia the effect was pronounced on the bluish gray iris. In the subjects with neurovegetative dystonia the drugs acted without any relation to the color of the iris.

H. F. CARRASQUILLO.

OCULAR CHANGES IN FIFTY CASES OF GENERAL PROGRESSIVE PARALYSIS. E. ANDROGUE and J. TELTAMANTE, Arch. de oftal. de Buenos Aires **19:** 8 (Jan.) 1944.

Fifty cases of general progressive paralysis were studied in relation to their ocular changes. Disturbances of the photomotor reflex were exhibited in 68 per cent of cases. The Argyll Robertson pupil was present in 20 cases, in 10 of which the pupils were miotic, in 5 normal and in 5 mydriatic. In 6 per cent there was total pupillary rigidity. In all cases the action on the iris of pilocarpine, homatropine, physostigmine and atropine was evident.

H. F. CARRASQUILLO.

OPTICOCHIASMIC ARACHNOIDITIS. A. ANDROGUE and M. DIEZ, Arch. de oftal. de Buenos Aires **19:** 20 (Jan.) 1944.

A statistical study of the symptomatology of this condition was made, with the purpose of evaluating each symptom. Forty cases were

analyzed in which operation was performed, and a synopsis of the clinical and laboratory data in each case is given.

Males predominated (65 per cent). The ages ranged from 13 to 62 years, most of the patients being between 13 and 45 years of age.

Syphilis and trauma were the causative factors in 50 per cent of the cases. Intrinsic motility was preserved in 52.5 per cent, and the reflexes were disturbed in 18 per cent. Optic nerve atrophy was present in 52.5 per cent. Visual acuity was diminished in 85 per cent. In the field study, scotomas were present in 37.5 per cent of cases and a concentric contraction in 30 per cent. In 29 cases the diagnosis was proved by exploration of the chiasmic region, and in 10 cases, by subtemporal decompression; in 2 cases the diagnosis was made clinically.

Early surgical treatment is advocated. H. F. CARRASQUILLO.

Ocular Muscles

SUMMARY OF REEXAMINATION OF ORTHOPTIC PATIENTS WITH CONSIDERATION OF PERMANENCE OF RESULTS. J. S. ROBINSON, Am. J. Ophth. **28:** 999 (Sept.) 1945.

Robinson concludes (1) that the potential response of each patient is a deciding factor in the permanent result, (2) that the limitations of orthoptic treatment must be realized and (3) that with such therapy the tendency of an eye to deviate is often not eliminated but, rather, the ability to overcome this tendency is strengthened so that the deviation is not troublesome. Finally, he states that a good result depends on correct diagnosis and proper treatment by various methods in logical sequence.

W. S. REESE.

RESECTION OF THE INFERIOR OBLIQUE MUSCLE IN HYPOTROPIA. O. H. WAGMAN, Am. J. Ophth. **28:** 1220 (Nov.) 1945.

Wagman discusses resection of the inferior oblique muscle in cases of this imbalance and emphasizes the necessity of proper work-up of such cases. He reports a case in which he resected the inferior oblique, did a recession of the rectus internus and resected the rectus externus muscle.

W. S. REESE.

INVERTED BELL SIGN. M. MARIN AMOT, Arch. Soc. oftal. hispano-am. **4:** 534 (July-Aug.) 1944.

A case of an inverted Bell sign is reported. When the eyes were closed, the globe was turned down instead of moving upward, as in the usual Bell phenomenon, the synergy occurring between the closing of the lids and the depression of the eye. H. F. CARRASQUILLO.

Orbit, Eyeball and Accessory Sinuses

OPTICAL IRIDECTOMY ON SUBATROPHIC EYES. A. VON FILATOV, Vestnik oftal. **24:** 8, 1945.

Filatov reports 2 cases of war injury of the only eye in which optical iridectomy was done, with resulting ability to count fingers. He believes

that even in the presence of faulty light perception only the ophthalmologist should not give up and should give the patient the benefit of minimum vision, which is better than none.

Tissue therapy in the form of injections of preserved placenta tissue was given the patients for months before and after the operation.

O. SITCHEVSKA.

ENUCLEATIONS IN WARTIME. C. PTITZA, Vestnik oftal. **24:** 74, 1945.

During 1942 and 1943 714 operations on the eye were performed in the evacuation hospital. Of these, 52.3 per cent were penetrating ocular injuries, and the proportion of enucleations was high: 195 enucleations and 72 eviscerations. The enucleations of wartime differ from those of peacetime. The eyeball is frequently "smashed"; later, firm adhesions form with the muscles and orbit. Fragments are frequently found, and there are infected wounds near the eyeball, all of which factors make enucleation in wartime difficult and often dangerous, as it may be complicated by phlegmon, sinus thrombosis and meningitis. The author reports 2 cases of meningitis which followed enucleation in the absence of any clinical contraindications. Frequently fragments were removed when cutting the optic nerve; sometimes it was necessary to remove the fragments after the enucleation.

Sulfanilamide powder was always used for the conjunctival wound, and sulfonamide preparations were administered internally. In cases of wounded service men with serious general wounds, fever and undernourishment, enucleation was usually postponed until the general condition was improved. Enucleation was done in a few cases of injury to the skull with low grade meningoencephalitis; no complications were encountered.

O. SITCHEVSKA.

Refraction and Accommodation

TRANSIENT MYOPIA DURING TREATMENT WITH SULFANILAMIDE. C. BRITTO, Arq. brasil. de oftal. **5:** 35 (April) 1942.

The author presents a clinical observation on a patient who had taken 2 Gm. of sulfanilamide daily for eight days. At the end of this period headache, vomiting and loss of appetite appeared and the treatment was suspended, myopia being noted soon after. Visual acuity without correction was: 1/2 in each eye. Homatropine had no effect on refraction. The myopia gradually decreased, and eight days after the first examination visual acuity was 20/20, without correction.

A tabulation of 20 cases reported in the literature is presented. The various theories regarding pathogenesis are discussed, the author being inclined to accept that of spasm of accommodation.

A bibliography is included.

M. E. ALVARO.

Retina and Optic Nerve

PHOTO-RETINITIS IN ANTI-AIRCRAFT LOOKOUTS. JAMES FLYNN, M. J. Australia **2:** 400 (Oct. 31) 1942.

The author, a surgeon lieutenant commander with the Royal Australian Navy, observed that watchers at antiaircraft look-outs and similar

personnel have frequently to look directly into the sun. Four cases of photoretinitis in such men are reported. All had central scotomas of varying degrees, lowered visual acuity and round macular lesions. All had been looking through a "sunglass screen," which the author had not seen but assumed was inefficient. He believes that as a temporary expedient Crookes B2 lenses absorb enough infra-red rays to justify their use for protection but believes that standardized protective equipment should be devised and issued to the armed forces.

G. M. BRUCE.

Therapeutics

TISSUE THERAPY. V. P. Filatov, Vrach. delo 11: 499, 1945.

The basic method of tissue therapy is the transplantation of preserved tissue (skin of a living person or of the cadaver, placenta or other organs) for a period of six or seven days at a temperature of 2 to 4 C. into the skin of the recipient. The sterilization of the preserved tissue in the autoclave at a temperature of 120 C. does not deprive the tissue of its therapeutic action. Filatov therefore uses at present implantation (instead of transplantation) of tissue material into a skin pocket or under the conjunctiva. The material may be homogenous, autogenous or heterogenous.

The implantation may be repeated every two or three weeks. Filatov and his school also used subcutaneous injections of aqueous extracts of the preserved tissue. He also employed for the first time injections of extract of preserved leaves of aloe (kept in the dark for fifteen days), as in his opinion they contain biogenic stimulators. Cerebrospinal fluid from the cadaver, aqueous humour from cattle, cod liver oil and stored autoblood were also used. The technic of the preparation of the tissue, of aqueous extract and of the green leaves of plants is given in detail.

Tissue therapy gave excellent results with many diseases of the eye. Improvement of trachomatous pannus was observed in hundreds of cases as a result of injections of extracts and implantation of preserved, autoclaved material under the skin or the conjunctiva. Tissue therapy was also effective in the treatment of interstitial keratitis (of syphilitic origin) and tuberculous and herpetic keratitis. Recurrence and the acute symptoms were abolished with tissue therapy. In a number of cases of uveitis and opacities in the vitreous improvement followed tissue therapy. In cases of uveitis tissue therapy was frequently combined with autohemotherapy and specific treatment.

About 150 patients with retinitis pigmentosa were given tissue therapy. The visual acuity, the visual fields and dark adaptation (measured with the adaptometer) were increased to a striking degree. The night blindness disappeared in a few cases. The chorioretinitis of myopia responded to tissue therapy to a certain degree. In some cases there were increase of vision and decrease of central scotomas. The hemorrhages and opacities in the vitreous absorbed much faster than when no treatment was employed.

O. SITCHEVSKA.

Society Transactions

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Feb. 18, 1946

Retrolental Fibroplasia in Premature Infants: Terry's Syndrome. DR. OLGA SITCHEVSKA (by invitation).

Terry (*Am. J. Ophth.* 25: 1409-1423, 1942) has given the following salient clinical characteristics of retrolental fibroplasia: 1. The condition occurs in about 12 per cent of premature babies who weigh 3 pounds (1,360 Gm.) or less. 2. There is an opaque, vascularized membrane behind the lens, a growth of embryonic connective tissue. 3. The anterior chambers are shallow or absent. 4. The condition is bilateral. 5. The color of the iris is "fetal blue" and changes slowly to muddy gray or brown. 6. Thin ciliary processes can be seen in front of the opaque membrane. 7. The eyes have a searching nystagmus. 8. The eyes are usually small.

Dr. Terry has examined periodically about 100 babies with retrolental fibroplasia and knows of about 300 infants with the condition.

Two cases were presented.

Both babies were born prematurely, at the fetal age of 6½ months, and weighed less than 3 pounds. In the case of the male infant the diagnosis of retinoblastoma was first made and later changed to retrolental fibroplasia. Examination of the righ eye showed posterior synechias, absence of the anterior chamber and increased tension, with no response to mydriatics. The left eye had a shallow anterior chamber, and on dilatation a grayish, vascularized membrane could be seen above. The child was about 2 years old at the time of the report, and his physical and mental development was normal. The tension appeared normal in both eyes (without medication). The irises were of a "fetal blue" color, but the left eye was beginning to turn to a muddy brown. The eyes were rather large.

The female baby had very small eyes. The right eye showed searching nystagmus and posterior synechias; the left eye dilated freely, and a gray membrane could be seen behind the lens, which thinned considerably during the period of observation. At the time of the report the grayish membrane appeared like heavy opacities of the vitreous. Intraocular tension had been normal.

Neither baby had any light projection. Both infants were seen by Dr. Terry, who confirmed the diagnosis of retrolental fibroplasia.

DISCUSSION

DR. RUTH MORRIS BAKWIN: Retrolental fibroplasia is of great interest to the pediatrician. To what extent this condition affects the mental development of the child is not known. One of the patients presented by Dr. Sitchevska had an intelligence quotient of 128, one of superior intelligence, on the interim Hayes-Binet test.

In the past decade this condition has increased out of proportion to the rate of survival of premature infants. The mortality rate has remained at about the same level since 1933—25 to 26 per hundred thousand of the population.

Of the 150 patients reported by Dr. Reese and Dr. Terry, 95 were males and 55 females. If this ratio is borne out by other studies, it would seem that retrolental fibroplasia is sex linked.

Construction of Lacrimal Passage: Report of a Case and Discussion of Experience with the Procedure. DR. LOREN P. GUY.

The case of a Sicilian woman aged 26 for whom was constructed a new lacrimal passage is presented and illustrated with lantern slides. The surgical technic employed was similar to that presented to this society on Dec. 15, 1941, and published later (Surgical Construction of a Lacrimal Passage, ARCH. OPHTH. 29: 575-577 [April] 1943) except that a skin graft was used instead of a mucous membrane graft, since the latter was not readily available. The skin graft took well in spite of there being unexpected infection in the ethmoid cells, and the patient had a patent lacrimal passage at the time of the report, five months after the operation. This passage was about 75 per cent as efficient as a normal natural passage.

The patient had had five operations on the lacrimal passage, the first consisting in probing at the age of 4 months. The lacrimal sac had been removed, and there was a disfiguring scar over the area. Removal of this scar tissue has improved the appearance of the ocular region.

A lacrimal passage lined with skin epithelium will remain patent, but if mucous membrane is available it is the tissue of choice.

DISCUSSION

DR. OSCAR GREGOR: The use of an elastic hollow rubber catheter is an improvement in the surgical technic of replacement of a lacrimal passage. Royales, of Madrid, and Morax used nonelastic wax around which a graft was wrapped. The method was disappointing; to quote Dr. S. A. Gifford: "The Morax method of employing a Tiersch graft wound around a small peg is difficult and often unsuccessful." Apparently, the graft must be exposed to proper pressure, and the compressibility of the hollow rubber tube furnishes this. McWilliams (Principles of the Four Types of Skin Grafting, J. A. M. A. 83: 183 [July 19] 1924) stated: "Pressure is the keynote of success in using free grafts, being next to asepsis in importance."

Mucous membrane seems superior to skin as a source of a graft in this situation, as skin remains skin and exfoliation of the keratinized areas may endanger the free passage. However, the resistance that the skin in the case reported had to infection must be borne in mind, and the use of the skin graft must be reappraised in the light of future experience.

DR. HENRY E. BRANCA: The diagnosis of right-sided acute purulent ethmoiditis was made at the time of operation, for when the opening was made into the nose and some of the ethmoid cells were ruptured there was a free discharge of pus into the wound. I was asked to treat the nose after operation, but I was unable to institute therapy until the

rubber catheter was removed, on the sixth day. At that time an intranasal examination revealed free pus in the right nasal cavity with a similar, but less severe, condition on the left side. After the pus had been suctioned out and the nasal membranes shrunk, examination revealed in the region of the agger nasi a small prominence of grayish tissue, which probably represented the graft; the middle meatus presented mucopus. The patient had the symptoms and signs of acute ethmoiditis. We treated the patient daily with the Proetz displacement method and with the application of astringents to the middle meatus. It took about twelve days for the ethmoiditis to clear up, and we were fortunate in getting the graft to take. I should like to believe that the care of the sinus condition played a role in bringing about the "take" of the graft.

Retrolental Fibroplasia. Dr. Arlington C. Krause, Chicago.

A summary of 18 cases of congenital encephalo-ophthalmic dysplasia of unknown origin was given. The ocular disease was similar to, or identical with, the retrolental fibroplasia described by Terry.

This dysplasia was more commonly found in premature infants and in infants from a multiple birth. The common neurologic signs in many cases were mental retardation, microcephalus and hydrocephalus. Mental retardation was frequently evidenced when the child became several years old. Postmortem examinations in 2 cases revealed hypoplasia, hyperplasia and heterotopias of the cerebrum and cerebellum and internal hydrocephalus.

The ocular signs were loss of vision, ptosis, endophthalmos, microphthalmos, strabismus, retinal detachment, retrolental masses, retinal atrophy and gliosis, retinal dysplasia, coloboma of the choroid and optic nerve, recurrent hemorrhages in the retina and vitreous, anterior and posterior synechias, secondary glaucoma and cataract.

In the more severe form of the disease, the child died of intercurrent infection or was placed in an institution for the feebleminded.

DISCUSSION

Dr. Algernon B. Reese: May I point out the features of Dr. Krause's contribution about which I feel there might be some room for disagreement? Although I do not agree with him on some of the fundamental aspects of his concept, his work is a stepping-stone toward a better understanding of this most vexing problem.

As Dr. Krause has pointed out, for one hundred years or more basically related lesions have been reported under various synonyms, such as co-called persistent tunica vasculosa lentis, congenital membrane behind the lens and congenital connective tissue in the vitreous. These lesions formerly were rare. At our hospital my colleagues and I saw about 1 case every two years. They were usually in full term infants and were frequently unilateral. In the past decade the frequency has increased a great deal. We now see from 6 to 12 cases a year or more; the condition is usually bilateral and is more frequent in premature infants. Because of this increased incidence a great deal of attention has been given to the subject of late. More recently, Terry has described the anomaly occurring in premature babies as retrolental

fibroplasia. He felt that the lesion was acquired and that it was different from the condition which had been seen rather infrequently in the past. Dr. Frank Payne and I (Persistence and Hyperplasia of the Primary Vitreous, *Am. J. Ophth.* **29:** 1-24 [Jan.] 1946) stated the belief that the abnormality in these erstwhile sporadic cases and that in the more recent cases occurring in premature babies were one and the same basic lesion and that it represented the congenital remains of an angioblastic mesoderm composing the primary vitreous and occurring with or without hyperplasia. We concluded that the increased incidence was due to the lowered mortality of premature infants, but Dr. Bakwin's comments this evening lead me to the belief that we may have been wrong in this assumption.

Is the ocular lesion which Dr. Krause describes the same as that which Terry and Payne and I have described? I have seen Dr. Krause's illustrations, and I feel confident that we are all speaking of the same condition. Terry, calling the lesion retrolental fibroplasia, concluded it was an acquired manifestation and explained it on this basis. Payne and I, designating the lesion as persistence and hyperplasia of the primary vitreous, expressed the belief that the lesion represented congenital remains and hyperplasia of tissue which should have disappeared. Dr. Krause, calling the lesion congenital encephalo-ophthalmic dysplasia, believes it represents a faulty development of the neuroectoderm in that portion where it forms the retina as well as the brain.

First, Dr. Krause claims that the ocular lesion is a primary dysplasia of the retina. However, it seems to me that he does not explain the almost constant appearance of fibrous tissue in the vitreous. I cannot conceive of this fibrous tissue being secondary to a retinal dysplasia. Payne and I demonstrated in this fibrous tissue of the vitreous the presence of cartilage, smooth muscle, fat, connective tissue and blood vessels—in other words, all the derivatives of the mesoderm. This being true, it would seem that the fibrous tissue must represent a primary lesion in the vitreous. The presence of the hyaloid artery is a fairly common occurrence in these cases, and I cannot see how this fits into the picture of the retinal dysplasias. Hemorrhage is a frequent occurrence, and I do not see how hemorrhage can stem from dysplasia.

In Dr. Krause's first illustration he showed a microscopic section in which the retina extended rather far forward, and he spoke of this as a hyperplasia. It seemed to me that this retina extended forward to some fibrous tissue which was back of the lens, in the neighborhood of the equator.

The microscopic sections in which he showed that there was no evidence of fibrous tissue back of the lens I regard as inconclusive; because serial sections (or at least sections throughout the area of the lens) should be made to rule out the presence of this fibrous tissue. In order to identify this fibrous tissue clinically, it is sometimes necessary to stand on your head, so to speak, in order to obtain a view sufficiently far to the periphery to appreciate the presence of the tissue at the equator of the lens.

Second, Dr. Krause says that mental retardation, resulting from dysplasia or agenesis of the brain, is a part of the picture. (Perhaps one should define "mental retardation" to avoid a misunderstanding

in terms.) Except for 4 cases of hydrocephalus, which I feel it would be misleading to include, there was evidence of mental retardation in only 5 (or 30 per cent) of his cases. This incidence is no higher than that in the series of cases of cataract associated with rubella. Moreover, prematurity itself and cerebral anoxia (a condition figuring in a surprisingly large number of Dr. Krause's cases) predispose to a higher than normal incidence of mental retardation. In 82 per cent of Dr. Krause's cases the babies were premature. If the 2 cases of cerebral agenesis (diagnosis not supported by autopsy observations) are also included with the cases of mental retardation in his series, that category would comprise 7 cases (or 38 per cent). On the basis of his evidence, it is not necessary to postulate cerebral agenesis to explain the slower development of these children. I wrote letters inquiring about the mental development in all the accessible cases in the series Dr. Payne and I reported. I had 18 replies, and 16 stated that the child was normal, i. e., that it had developed at the same pace as any other child of the same age. Only 2 (or 11 per cent) of the 18 children were mentally retarded. I do not believe that Dr. Krause's findings justify him in the assumption that mental retardation is a usual accompaniment of the ocular lesion we are discussing tonight.

Lastly, what evidence of cerebral dysplasia or agenesis do Dr. Krause's cases show? Except for the cases of hydrocephalus, in some of which autopsies were performed, there was only 1 case in which a complete autopsy report is given, including microscopic observations. This was case 10, which I feel does not belong in this category because the eyes, in my opinion, do not show the lesion under discussion.

DR. BRITTAIN F. PAYNE: I have brought two or three slides to illustrate in the human embryo some features of the background of the anomaly which has been so beautifully described here. Some one should review the development of the human eye for us, so that we may appreciate these points. Dr. Reese calls this anomaly a developmental abnormality of the primary vitreous. I am not sure that I understand exactly what he means by primary vitreous. My interpretation of primary vitreous is, or at least it was a few years ago, simply that of fibers extending from the surface ectoderm to the neural ectoderm, and these fibers are truly the anlagen of the vitreous body. The secondary and the tertiary vitreous body are formed by mesoderm which comes in through the cleft, but also is fixed at a base, which later is located on the flat part of the ciliary body. The first slide shows the primary optic vesicle with the surface ectoderm thickening to form the lens plate, which is to come off and contribute the invagination. The next slide shows the invagination to form the secondary optic vesicle, and the lens vesicle is detached from the surface ectoderm. The fibrils extending from it to the primitive retina are, as I understand it, the primary vitreous body. The next stage has to do with the ingrowth of the mesoderm, which goes to form the secondary and the tertiary vitreous. While this process is going on, the central retinal vessels come in through the nerve and extend up to the lens vesicle, as shown in the next section. One can see here the hyaloid system with the vessels surrounding the lens itself. If for some reason, a child were born at this age, it would weigh under 3 pounds, and the chances are that

in the organization of this central retinal system one would have the formation of a membrane which would correspond to the one described by Terry; unless one considers that the hyaloid artery is a part of the vitreous, I do not see how one can arrive at any definite conclusion about it. In other words, it would have to be a part of the vitreous body if we consider it as Dr. Reese explained it, and not a part of the remnants of the hyaloid system.

DR. BLANCHE JACKSON, Boston: My associates and I have been working on the animal aspect of the problem primarily and have tried to find something which would produce the condition of retrolental fibroplasia in animals. Warkany's work on vitamin A deficiency in the rat has been repeated in our laboratory, and we have verified his finding that in this species the offspring of vitamin A–deficient mothers may show a fibroplasia-like growth of mesenchyme in the vitreous.

DR. ARLINGTON C. KRAUSE, Chicago: I think the cause of the fibroplasia, or whatever the condition is, is the answer to our questions. There are many questions I should like to ask Dr. Reese about the primary vitreous. Is it part of the retina or not? And its hyperplasia—would that fall in with a retinal dysplasia or not?

It is fortunate that Terry has focused interest on this disease and brought it to the attention once more. Many patients will have to be seen and the origin and outcome of their condition studied.

I regret that I cannot answer all of Dr. Reese's questions: That would require reading my paper again. A large number of children with this condition do have something wrong with their neural ectoderm, whether it ends in mental retardation or leads to their being institutionalized, as have 4 of my series up to the present time, not for their eyes, but for their low mentality. If one includes the hydrocephalic and the microcephalic cases, as Dr. Reese does not, the group in which there is some mental aberration becomes rather large. I have been wondering whether there are not three types of fibroplasia—the Boston, the Knickerbocker and the midwestern. There may be a particular form of the disease in the particular locality. In Chicago one sees many detached retinas. In Boston Terry apparently has many cases of persistent hyaloid artery, and Dr. Reese frequently sees fibroplasia of the vitreous. If, in considering the cases of rubella, as Dr. Reese has, and as I have recently done, one notes a change in what this disease does to the child in utero. Such a child is affected very early, and the disease produces certain anomalies of the eye, which are more than mere cataract. It also affects the body in general, as is generally recognized, and there are cases of rubella in which low tone deafness, defects of the interventricular septum and other disturbances, such as—I dislike to say it again—mental retardation and microencephaly, are produced.

I am very much in accord with Dr. Reese that all cases of fibroplasia do not appear in premature infants and that the disease may be unilateral; the infant is born with the disease, actually or potentially—actually, in the sense that the disorder may appear at birth, or potentially, in that it may develop afterward, because the seeds of the

disorder are there. In the discussion on the paper by Dr. Reese and Dr. Payne, Ida Mann summarized fibroplasia well in one sentence:

> These cases are all good examples of the general principle of the production of developmental anomalies through the arrest at a definite stage of intra- or extra-uterine life followed by aberrant growth.

This is another reason that I have called the disease congenital ophthalmic dysplasia.

COLLEGE OF PHYSICIANS OF PHILADELPHIA, SECTION ON OPHTHALMOLOGY

Burton Chance, M.D., *Chairman*

George F. J. Kelly, M.D., *Clerk*

March 21, 1946

Vascular Disease Associated with Angioid Streaks of the Retina and Pseudoxanthoma Elasticum.

This paper was published in the March 1946 issue of the ARCHIVES, page 241.

DISCUSSION

DR. FRANCIS HEED ADLER: The thesis of this communication is well founded, i. e., that angioid streaks of the retina, osteitis deformans, pseudoxanthoma elasticum and some forms of peripheral vascular disease are parts of the same clinical entity, which is not as yet completely elucidated.

The pathology of the arteries is not entirely clear, as is evidenced by the fact that a number of pathologists to whom these sections were shown were somewhat puzzled by them. The general consensus seems to have been that the disease process was confined to the elastic tissue of the arteries. It seems strange that no one had previously made a study of the changes in the elastic tissue of the arteries associated with angioid streaks of the retina, although it was mentioned in the literature that such changes might be present.

These observations tend to confirm the opinion that the underlying pathologic process of angioid streaks in the retina is a degeneration of the elastic tissue of Bruch's membrane.

DR. GEORGE F. J. KELLY: I should like to ask Dr. Scheie whether he had much to do with getting this section of artery. After all, this artery was a little patulous. After he removed the piece, was there enough collateral circulation to carry on? I mean to say, one can get sections of skin but a section of an artery is a bit unusual.

DR. FRANK B. WALSH, Baltimore: It is interesting that pseudoxanthoma elasticum was associated with angioid streaks in all the cases described. How frequently have the authors seen angioid streaks in the absence of changes in the skin?

MAJOR HAROLD SCHEIE, Medical Corps, Army of the United States: In answer to Dr. Kelly, we took the biopsy specimen with little hesitation because the ulnar artery was completely occluded. Microscopic evidence further justified taking the specimen by verifying the occlusion.

The wall of the artery and the tissues surrounding the artery showed newly formed and anastomotic vessels as large as the very minute residual lumen of the ulnar artery. The presence of a residual lumen was even debatable. When the artery was examined several sections higher, what seemed to be residual lumen at the lower level had shifted to one side and looked like any of the anastomotic vessels. Furthermore, the patient being an extremely intelligent soldier, the situation was explained to him. He was told that he would derive no benefit from the procedure but that we were desirous of obtaining further information which might possibly be of aid to others in the future.

In answer to Dr. Adler's question, clinical disease of the peripheral vessels is not mentioned in the literature. Scholz did mention absence of the peripheral pulse in 1 patient, but apparently he considered it no further.

Several references to degeneration of elastic tissue in arterial walls were found as part of routine microscopic studies.

Symptomatology of Subdural Hematomas in Infants and in Adults with Particular Reference to Ocular Signs: Observations on Pathogenesis of Subdural Hematoma. DR. CLIFTON D. GOVAN and DR. FRANK B. WALSH, Baltimore.

This paper will be published in a future issue of the ARCHIVES.

Book Reviews

Ophthalmia Neonatorum: The Problem After Thirty Years of Statutory Notification and Sixty Years of Credé Prophylaxis. Institute of Ophthalmology Monographs no. 1. By Arnold Sorsby, M.D., F.R.C.S. Price not given. Pp. 66. London: Hamish Hamilton, Ltd., 1945.

All children who suffer from ophthalmia neonatorum in the County of London are admitted to the hospital of the London County Council, of which Professor Sorsby is the ophthalmic surgeon. His experience is therefore unique, and a monograph on this subject from his pen is, of course, completely authoritative.

Since 1914 notification of a purulent discharge from the eyes of a newborn infant has been compulsory in England and Wales. This booklet is a study of the problem of ophthalmia neonatorum. It is composed largely of tables, charts and graphs, and is therefore difficult to review and well nigh impossible to abstract. Nevertheless, many of the conclusions reached by the author are worth recording here. His approach is sound. He admits that the rates recorded by the Registrar General, consistent though they be, are not an unquestionable indication of the incidence of ophthalmia neonatorum; and he remarks that notification is designed for the purpose of insuring early and adequate treatment, not that of collecting statistics. He finds, however, that the incidence of blindness in children has declined considerably but is not convinced that this is due alone to the concurrent decline in the incidence of ophthalmia neonatorum. He shrewdly points out that other ophthalmias, notably the phlyctenular and syphilitic types, have also become less frequent.

It is interesting to note the revolution in opinion where etiology of conjunctivitis in the newborn is concerned. Originally, of course, the term "ophthalmia neonatorum" was practically synonymous with "gonorrheal conjunctivitis." Now the advances in bacteriologic investigation and the emergence of blennorrhea as a clinical entity have negated, and very nearly reversed, this conception. For example, a table listed 37 cases of ophthalmia neonatorum reported in 1914, in 20 of which the disease was gonococcic in origin. In the same table, in 1935, 37 cases are again reported, in none of which gonorrhea was present. Professor Sorsby finds that the most frequent cause is the staphylococcus (35 per cent). He places the gonococcus next (25 per cent) and viruses next (10 per cent).

The role played by prophylaxis in the reduction of this disease is well discussed, and some interesting conclusions are drawn. The author finds no evidence that silver nitrate is superior to some of the organic silver preparations, and he states that it calls for more care in its use. He draws attention to the instability of this disinfectant and advocates that it be supplied in paraffin-lined yellow wax (beeswax) capsules or other suitable containers.

The discussion of changing methods of therapy and their increasing efficacy is, in the opinion of this reviewer, the most important contri-

bution of this work. When sulfonamide therapy was introduced, it was approximately four times as effective in a given time as were the older, local, procedures. Later, the advent of penicillin relegated all other methods of cure to the background, and indeed rendered them obsolete. The author says: "The reduction of the duration of treatment from weeks by the older methods to days by the sulphonamides is paralleled by the reduction of treatment from several days by the sulphonamides to as many hours by penicillin."

The method of use of penicillin is as follows:

1. On admission a swab is taken for smear and culture, and the eye is irrigated with half-normal saline solutions at room temperature. A drop of epinephrine hydrochloride (1 : 1,000) is instilled and a scraping taken from the palpebral conjunctiva for examination for inclusion bodies.

2. Pus is wiped away, and 1 drop of penicillin in a concentration of 2,500 units per cubic centimeter is instilled.

3. These instillations are repeated every five minutes until there is no discharge. Generally, a half-hour's to three hours' treatment is all that is needed. Pus is disregarded, and no irrigations are necessary.

4. When there is no longer any discharge, penicillin is instilled at half-hour intervals. In about six to twelve hours the eyes appear normal, but the penicillin is continued hourly for twelve hours and every two hours for twenty-four hours thereafter.

The author closes by pointing out that the advocacy of Gibson, made nearly fifty years before Credé, that the disease in the mother should be eradicated before parturition, is still largely unachieved.

This monograph has consigned to a deserved oblivion many of the older theories of ophthalmia neonatorum and has brought the subject completely up to date. It should, of course, be studied by all ophthalmologists; but obstetricians, bacteriologists and public health officers will also find that it can be read with profit to themselves and their charges.

G. M. BRUCE.

Journal of the History of Medicine and Allied Sciences. Volume 1, number 1. Subscription, $7.50 in the United States, Canada and Latin America. Pp. 132. Quarterly. New York: Henry Schuman, January 1946.

The field of our science is so wide, its relations with other activities and interests of mankind so numerous and important, that one might well paraphrase the classic sentence to read "*medicus* sum, et humani nihil a me alienum puto." The appearance of a quarterly on the history of medicine is significant as a contribution to present day culture and the store of knowledge. No exposition of the *raison d'être* and purpose of this publication could have been more clear and instructive than that of the editor, George Rosen, in his timely and interesting prologue to the initial number of volume 1.

The medical thought of the past is, indeed, an important element in the training of the physician and his collaborators, professional and lay, especially in times like the present. There is in the United States only one other publication in this field, the *Bulletin of the History*

of Medicine, edited by Siegerist. The *Journal* will supplement, rather than compete with it, and it welcomes, as it now presents, contributions on such aspects of the subject as public health, nursing, pharmacy, veterinary medicine and dentistry, as well as biographies of outstanding workers in these fields and in the many arts and sciences that impinge on medicine.

The table of contents lists chapters on "Animal Substances in Materia Medica" (MacKinney), "Galenicals of Vesalius" (Singer), "Pharmacopoeias in World History" (Urdang), "Earliest Dentistry Wood-Cuts" (Proskauer), "Incubator and Taboo" (Ackerknecht), "Medical Education in 17th Century England" (Phyllis Allen); and biographic notes on William Blake and John Hunter (Jane Oppenheimer) and on Waterhouse, Harrison, and de Monserrate, author of the first anatomy in the Spanish language (Saunders and O'Malley). "Notes and Queries" (editor, Fisch) and "Book Reviews" deal with similar topics and personalities.

This is rich fare, indeed, and holds much of interest for those who have leisure and inclination to browse in the highways and byways (Gifford) of medicine. Many of the chapters are richly illustrated with woodcuts from old treatises and manuals. In this connection, it is a matter of regret that most of the reproductions are on too small a scale and are badly reproduced. The paper stock may in part be responsible for this shortcoming. While it is matt, free from glare, and so, very easy on the eyes it, unfortunately, allows the ink to spread so that not a few minor details are lost. This applies as well to the text of subtitles and explanatory notes, especially those in Latin or in German (Gothic) type, which would add so greatly to the pleasure of medicohistorical study if they were not practically illegible. If in future issues of the journal these illustrative woodcuts were reproduced on special (calendered?) paper and, if possible, on a larger scale, little would be lacking for full enjoyment of this artistically and culturally valuable publication.

PERCY FRIDENBERG.

News and Notes

EDITED BY DR. W. L. BENEDICT

GENERAL NEWS

Alumni Meeting of New York Eye and Ear Infirmary.—The first alumni meeting of the New York Eye and Ear Infirmary since the war will be held at 9 a. m., Sept. 7, 1946, at the New York Eye and Ear Infirmary, to be followed by a dinner at the University Club the same evening.

Communications should be addressed to B. F. Payne, M.D., acting secretary-treasurer, New York Eye and Ear Infirmary, 218 Second Avenue, New York 3.

Directory of Ophthalmologic Societies *

INTERNATIONAL

International Association for Prevention of Blindness

President: Dr. P. Bailliart, 66 Boulevard Saint-Michel, Paris, 6e, France.
Secretary-General: Prof. M. Van Duyse, Université de Gand, Gand, Prov. Ostflandern, Belgium.
All correspondence should be addressed to the Secretariat, 66 Boulevard Saint-Michel, Paris, 6e, France.

International Ophthalmologic Congress

President: Prof. Nordenson, Serafimerlasarettet, Stockholm, Sweden.
Secretary: Dr. Ehlers, Jerbanenegade 41, Copenhagen, Denmark.

International Organization Against Trachoma

President: Dr. A. F. MacCallan, 17 Horseferry Rd., London, England.

Pan-American Congress of Ophthalmology

President: Dr. Harry S. Gradle, 58 E. Washington St., Chicago.
Executive Secretaries: Dr. Conrad Berens, 35 E. 70th St., New York. Dr. M. E. Alvaro, 1511 Rua Consolacão, São Paulo, Brazil.
Place: Habana, Cuba. Time: February 1948.

FOREIGN

All-India Ophthalmological Society

President: Dr. B. K. Narayan Rao, Minto Ophthalmic Hospital, Bangalore.
Secretary: Dr. G. Zachariah, Flitcham, Marshall's Rd., Madras.

British Medical Association, Section on Ophthalmology

President: Dr. W. Clark Souter, 9 Albyn Pl., Aberdeen, Scotland.
Secretary: Dr. Frederick Ridley, 12 Wimpole St., London, W. 1.

Chengtu Ophthalmological Society

President: Dr. Eugene Chan.
Secretary: Dr. D. S. Shen, Eye, Ear, Nose and Throat Hospital, Chengtu, Szechuan, China.
Place: Eye, Ear, Nose and Throat Hospital, Chengtu, Szechuan, China.

Chinese Ophthalmology Society

President: Dr. C. H. Chou, 363 Avenue Haig, Shanghai.
Secretary: Dr. F. S. Tsang, 221 Foochow Rd., Shanghai.

Chinese Ophthalmological Society of Peiping

President: Dr. H. T. Pi, Peiping Union Medical College, Peiping.
Secretary: Dr. C. K. Lin, 180 Hsi-Lo-yen Chienmeng, Peiping.
Place: Peiping Union Medical College, Peiping. Time: Last Friday of each month.

* Secretaries of societies are requested to furnish the information necessary to make this list complete and keep it up to date.

Faculty of Ophthalmologists

President: Brig. Sir Stewart Duke-Elder, 63 Harley St., London, W. 1, England.
Secretary: Mr. Frank W. Law, 45 Lincoln's Inn Fields, London, W. C. 2, England.

German Ophthalmological Society

President: Prof. W. Lohlein, Berlin.
Secretary: Prof. E. Engelking, Heidelberg.

Hungarian Ophthalmological Society

President: Prof. I. Imre, Budapest.
Assistant Secretary: Dr. Stephen de Grósz, University Eye Hospital, Máriautca 39, Budapest.
All correspondence should be addressed to the Assistant Secretary.

Midland Ophthalmological Society

President: Dr. W. Niccol, 4 College Green, Gloucester, England.
Secretary: Mr. T. Harrison Butler, 61 Newhall St., Birmingham 3, England.
Place: Birmingham and Midland Eye Hospital.

North of England Ophthalmological Society

President: Mr. E. F. Wilson, 24 Upper Northgate St., Chester.
Secretary: Mr. William M. Muirhead, 70 Upper Hanover St., Sheffield 3.
Place: Manchester, Leeds, Newcastle-upon-Tyne, Liverpool, Sheffield and Bradford, in rotation. Time: October to May.

Ophthalmological Society of Australia

President: Dr. J. Ringland Anderson, Astor House, 108 Collins St., Melbourne, Victoria.
Secretary: Dr. D. A. Williams, 27 Commonwealth St., Sydney.
Place: Melbourne. Time: Oct. 20-26, 1946.

Ophthalmological Society of Egypt

President: Prof. Dr. Mohammed Mahfouz Bey, Government Hospital, Alexandria.
Secretary: Dr. Mohammed Khalil, 4 Baehler St., Cairo.
All correspondence should be addressed to the secretary, Dr. Mohammed Khalil.

Ophthalmological Society of Hospital de Nuestra Señora de la Luz

Chairman: Dr. Manuel J. Icaza y Dublán, México, D. F., Mexico.
Secretary: Dr. Jorge Meyrán, México, D. F., Mexico.

Ophthalmological Society of South Africa

President: Dr. A. W. Sichel, National Mutual Bldg., Church Square, Cape Town.
Secretary: Dr. J. K. de Kock, Groote Kerk Bldg., 32 Parliament St., Cape Town.

Ophthalmological Society of the United Kingdom

President: Mr. Charles B. Goulden, 89 Harley St., London.
Secretary: Mr. Frank W. Law, 30 Devonshire Pl., London, W. 1.
Place: London. Time: May 30-June 1-2, 1946.

Ophthalmology Society of Bombay

President: Dr. D. D. Sathaye, 127 Girgaum Rd., Bombay 4, India.
Secretary: Dr. H. D. Dastur, Dadar, Bombay 14, India.
Place: H. B. A. Free Ophthalmic Hospital, Parel, Bombay 12. Time: First Friday of every month.

Oxford Ophthalmological Congress

Master: Mr. P. G. Doyne, 60 Queen Anne St., London, W. 1, England.
Secretary-Treasurer: Dr. F. A. Anderson, 12 St. John's Hill, Shrewsbury, England.
Time: July 4-6, 1946.

Palestine Ophthalmological Society

President: Dr. Arieh Feigenbaum, Abyssinian St. 15, Jerusalem.
Secretary: Dr. E. Sinai, Tel Aviv.

Polish Ophthalmological Society

President: Dr. W. Kapuściński, 2 Waly Batorego, Poznań.
Secretary: Dr. J. Sobański, Lindley'a 4, Warsaw.
Place: Lindley'a 4, Warsaw.

Revista Brasileira de Oftalmologia

President: Dr. Caldas Britto, Largo de Carioca 5-6° andar, Rio de Janeiro, Brazil.
Secretary: Dr. Evaldo Campos, R. Rodrigo Silva 7-1° andar, Rio de Janeiro, Brazil.
Place: Rio de Janeiro, Brazil. Time: Third Friday of every month from April to December.

Royal Society of Medicine, Section of Ophthalmology

President: Col. F. A. Juler, 96 Harley St., London, W. 1, England.
Secretary: Dr. Harold Ridley, 60 Queen Anne St., London, W. 1, England.

São Paulo Society of Ophthalmology

President: Silvio de Almeida Toledo, Barão de Ilapetininga St., 88, 5° Andar, São Paulo, Brazil.
Secretary: Dr. Plinio de Toledo Piza, Enfermaria Santo Luzia, Santa Casa de Misericordia, Cesario Motta, St. 112, São Paulo, Brazil.

Scottish Ophthalmological Club

President: Dr. S. Spence Meighan, 13 Woodside Pl., Glasgow, C. 3.
Secretary: Dr. Alexander Garrow, 15 Woodside Pl., Glasgow, C. 3.
Place: Edinburgh and Glasgow, in rotation.

Sociedad Argentina de Oftalmologia

Chairman: Dr. Jorge Malbrán, Buenos Aires.
Secretary: Dr. Benito Just Tiscornia, Santa Fe 1171, Buenos Aires.

Sociedad Oftalmologia del Litoral, Rosario (Argentina)

President: Prof. Dr. Carlos Weskamp, Laprida 1159, Rosario.
Secretary: Dr. Arturo Etchemendigaray, Villa Constitución, Santa Fé.
Place: Rosario. Time: Last Saturday of every month, April to November. All correspondence should be addressed to the President.

Sociedade de Oftalmología del Norte

President: Dr. Alberto Cárdenas.
Secretary: Dr. Jorge Luis Castillo, Mendoza 421, Tucumán, Argentina.

Sociedade de Oftalmologia de Minas Gerais

President: Prof. Hilton Rocha, Rua Rio de Janeiro 2251, Bello Horizonte, Minas Geraes, Brazil.
Secretary: Dr. Ennio Coscarelli, Rua Aimorés 1697, Bello Horizonte, Minas Geraes, Brazil.

Sociedade de Oftalmologia e Otorrinolaringologia de Rio Grande do Sul

President: Dr. Luiz Assumpção Osorio, Edificio Vera Cruz, Apartamento 134, Porto Alegre, Rio Grande do Sul.
Secretary: Dr. Fernando Voges Alves, Caixa Postal 928, Porto Alegre, Rio Grande do Sul.

SOCIEDADE DE OPHTHALMOLOGIA E OTO-RHINO-LARYNGOLOGIA DA BAHIA

President: Dr. Theonilo Amorim, Barra Avenida, Bahia, Brazil.
Secretary: Dr. Adroaldo de Alencar, Brazil.
All correspondence should be addressed to the President.

SOCIETÀ OFTALMOLOGICA ITALIANA

President: Prof. Dott. Giuseppe Ovio, Ophthalmological Clinic, University of Rome, Rome.
Secretary: Prof. Dott. Epimaco Leonardi, Via del Gianicolo, 1, Rome.

SOCIÉTÉ FRANÇAISE D'OPHTALMOLOGIE

Secretary: Dr. René Onfray, 6 Avenue de la Motte Picquet, Paris, 7e.

SOCIETY OF SWEDISH OPHTHALMOLOGISTS

President: Prof. K. G. Ploman, Stockholm.
Secretary: Dr. K. O. Granström, Södermalmstorg 4, III tr., Stockholm, Sö.

TEL AVIV OPHTHALMOLOGICAL SOCIETY

President: Dr. D. Arieh-Friedman, 96 Allenby St., Tel Aviv, Palestine.
Secretary: Dr. Sadger Max, 9 Bialik St., Tel Aviv, Palestine.

NATIONAL

AMERICAN MEDICAL ASSOCIATION, SCIENTIFIC ASSEMBLY, SECTION ON OPHTHALMOLOGY

Chairman: Dr. Derrick Vail, 55 E. Washington St., Chicago.
Secretary: Dr. R. J. Masters, 23 E. Ohio St., Indianapolis.

AMERICAN ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY, SECTION ON OPHTHALMOLOGY

President: Dr. Gordon B. New, Mayo Clinic, Rochester, Minn.
President-Elect: Dr. Alan C. Woods, Johns Hopkins Hospital, Baltimore 5.
Executive Secretary-Treasurer: Dr. William L. Benedict, 100–1st Ave. Bldg., Rochester, Minn.
Place: Palmer House, Chicago. Time: Oct. 13-18, 1946.

AMERICAN OPHTHALMOLOGICAL SOCIETY

President: Dr. John W. Burke, 1740 M St. W., Washington, D. C.
Secretary-Treasurer: Dr. Walter S. Atkinson, 129 Clinton St., Watertown, N. Y.

ASSOCIATION FOR RESEARCH IN OPHTHALMOLOGY, INC.

Chairman: Dr. Conrad Berens, 35 E. 70th St., New York.
Secretary-Treasurer: Major Brittain F. Payne, School of Aviation Medicine, Randolph Field, Texas.
Assistant Secretary-Treasurer: Dr. Hunter Romaine, 35 E. 70th St., New York.

CANADIAN MEDICAL ASSOCIATION, SECTION ON OPHTHALMOLOGY

President: Dr. Alexander E. MacDonald, 170 St. George St., Toronto 5.
Secretary-Treasurer: Dr. L. J. Sebert, 170 St. George St., Toronto 5.

CANADIAN OPHTHALMOLOGICAL SOCIETY

President: Walter W. Wright, 170 St. George St., Toronto 5.
Secretary-Treasurer: Dr. Kenneth B. Johnston, Suite 1, 1509 Sherbrooke St. W., Montreal.

NATIONAL SOCIETY FOR THE PREVENTION OF BLINDNESS

President: Mr. Mason H. Bigelow, 1790 Broadway, New York.
Secretary: Miss Regina E. Schneider, 1790 Broadway, New York.
Executive Director: Mrs. Eleanor Brown Merrill, 1790 Broadway, New York.
Place: New York. Time: Nov. 25-27, 1946.

SECTIONAL

ACADEMY OF MEDICINE OF NORTHERN NEW JERSEY, SECTION ON EYE, EAR, NOSE AND THROAT

President: Dr. Anthony Ambrose, 31 Lincoln Park, Newark.
Secretary: Dr. William F. Keim Jr., 15 Washington St., Newark 2.
Place: 91 Lincoln Park South, Newark. Time: 8:45 p. m., second Monday of each month, October to May.

CENTRAL ILLINOIS SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. Stuart Broadwell, 101½ N. 5th St., Springfield, Ill.
Secretary-Treasurer: Dr. William F. Hubble, 861-867 Citizens Bldg., Decatur, Ill.

CENTRAL WISCONSIN SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. P. G. Spelbring, 131 S. Barstow St., Eau Claire.
Secretary: Dr. G. L. McCormick, 650 S. Central Ave., Marshfield.

HAWAII EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. F. J. Pinkerton, 7 Young Hotel Bldg., Honolulu.
Secretary-Treasurer: Dr. L. Q. Pang, 52 S. Vineyard St., Honolulu 39.
Place: Honolulu. Time: Third Thursday of each month.

NEW ENGLAND OPHTHALMOLOGICAL SOCIETY

President: Dr. Howard F. Hill, 177 Main St., Waterville, Maine.
Secretary-Treasurer: Dr. Merrill J. King, 264 Beacon St., Boston 16.
Place: Massachusetts Eye and Ear Infirmary, 243 Charles St., Boston. Time: 8 p. m., third Tuesday of each month from November to April, inclusive.

PACIFIC COAST OTO-OPHTHALMOLOGICAL SOCIETY

President: Dr. D. H. O'Rourke, 1612 Tremont Pl., Denver.
Secretary-Treasurer: Dr. C. Allen Dickey, 450 Sutter St., San Francisco.

PUGET SOUND ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President: Dr. Julius A. Weber, 640 Stimson Bldg., Seattle 1, Wash.
Secretary-Treasurer: Dr. Barton E. Peden, 301 Stimson Bldg., Seattle 1, Wash.
Place: Seattle or Tacoma, Wash. Time: Third Tuesday of each month except June, July and August.

ROCK RIVER VALLEY EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. J. Sheldon Clark, Sterling, Ill.
Secretary-Treasurer: Dr. Harry R. Warner, 321 W. State St., Rockford, Ill.
Place: Rockford, Ill., or Janesville or Beloit, Wis. Time: Third Tuesday of each month from October to April, inclusive.

SAGINAW VALLEY ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. A. R. McKinney, 330 S. Washington St., Saginaw, Mich.
Secretary-Treasurer: Dr. Harold H. Heuser, 207 Davidson Bldg., Bay City, Mich.
Place: Saginaw or Bay City, Mich. Time: Second Tuesday of each month, except July, August and September.

Sioux Valley Eye and Ear Academy

President: Dr. J. C. Decker, 515 Francis Bldg., Sioux City, Iowa.
Secretary-Treasurer: Dr. J. E. Dvorak, 408 Davidson Bldg., Sioux City, Iowa.

Southern Medical Association, Section on Ophthalmology and Otolaryngology

Chairman: Dr. Savage Zerfoss, 165–8th Ave. N., Nashville 3, Tenn.
Secretary: Dr. Alston Callahan, 908 S. 20th St., Birmingham 5, Ala.
Place: Miami, Florida. Time: Nov. 6, 1946.

Southwestern Academy of Eye, Ear, Nose and Throat

President: Dr. H. L. Brehmer, 221 W. Central Ave., Albuquerque, N. Mex.
Secretary: Dr. A. E. Cruthirds, 1011 Professional Bldg., Phoenix, Ariz.

Southwestern Michigan Triological Society

President: Dr. W. M. Dodge, 716 First National Bank Bldg., Battle Creek.
Secretary-Treasurer: Dr. Kenneth Lowe, 25 W. Michigan Ave., Battle Creek.
Time: Last Thursday of September, October, November, March, April and May.

Western Pennsylvania Eye, Ear, Nose and Throat Society

President: Dr. J. V. Foster, State College.
Secretary-Treasurer: Dr. J. McClure Tyson, Deposit National Bank Bldg., Dubois.

STATE

Arkansas State Medical Society, Eye, Ear, Nose and Throat Section

President: Dr. E. C. Moulton, 619 Garrison Ave., Fort Smith.
Secretary: Dr. K. W. Cosgrove, 7 Urquhart Bldg., Little Rock.

Colorado Ophthalmological Society

President: Dr. George H. Stine, 23 E. Pikes Peak Ave., Colorado Springs.
Secretary: Dr. J. Leonard Swigert, 320 Republic Bldg., Denver.
Place: University Club, Denver. Time: 7:30 p. m., third Saturday of each month, October to May, inclusive.

Connecticut State Medical Society, Section on Eye, Ear, Nose and Throat

President: Dr. Paul B. MacCready, 442 Temple St., New Haven.
Secretary-Treasurer: Dr. W. H. Turnley, 1 Atlantic St., Stamford, Conn.

Eye, Ear, Nose and Throat Club of Georgia

President: Dr. William O. Martin Jr., Doctors Bldg., Atlanta.
Secretary-Treasurer: Dr. C. K. McLaughlin, 666 Cherry St., Macon.

Indiana Academy of Ophthalmology and Oto-Laryngology

President: Dr. W. E. Stewart, 721 Wabash Ave., Terre Haute.
Secretary: Dr. Russell A. Sage, 23 E. Ohio St., Indianapolis.
Place: French Lick. Time: First Wednesday in April.

Iowa Academy of Ophthalmology and Oto-Laryngology

President: Dr. S. A. O'Brien, 1 N. Federal Ave., Mason City.

Kansas State Medical Society, Section on Ophthalmology and Otolaryngology

President: Dr. W. B. Granger, Emporia.
Secretary: Dr. George F. Gsell, 911 Beacon Bldg., Wichita 2.

LOUISIANA-MISSISSIPPI OPHTHALMOLOGICAL AND OTOLARYNGOLOGICAL SOCIETY

President: Dr. George S. Adkins, 121 N. President St., Jackson, Miss.
Secretary-Treasurer: Dr. Edley H. Jones, 1301 Washington St., Vicksburg, Miss.

MEDICAL SOCIETY OF THE STATE OF PENNSYLVANIA, SECTION ON EYE, EAR, NOSE AND THROAT DISEASES

Chairman: Dr. William T. Hunt Jr., 1205 Spruce St., Philadelphia 7.
Secretary: Dr. Gabriel Tucker, 250 S. 18th St., Philadelphia 3.

MICHIGAN STATE MEDICAL SOCIETY, SECTION OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

Chairman: Dr. Edmond L. Cooper, 1553 Woodward Ave., Detroit 26.
Secretary: Dr. Ralph H. Gilbert, 110 Fulton St. E., Grand Rapids.

MINNESOTA ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. Karl C. Wold, 1051 Lowry Bldg., St. Paul 2.
Secretary: Dr. William A. Kennedy, 372 St. Peter St., St. Paul 2.
Time: Second Friday of each month from October to May.

MONTANA ACADEMY OF OTO-OPHTHALMOLOGY

President: Dr. H. Casebeer, 44 W. Park Ave., Butte.
Secretary: Dr. Fritz D. Hurd, 309 Medical Arts Bldg., Great Falls.

NEBRASKA ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. W. Howard Morrison, 1500 Medical Arts Bldg., Omaha.
Secretary-Treasurer: Dr. John Peterson, 1307 N St., Lincoln.

NEW JERSEY STATE MEDICAL SOCIETY, SECTION ON OPHTHALMOLOGY, OTOLOGY AND RHINOLARYNGOLOGY

Chairman: Dr. C. W. Buvinger, 50 Washington St., East Orange.
Secretary: Dr. Z. Laurence Griesemer, 1145 E. Jersey St., Elizabeth.

NEW YORK STATE MEDICAL SOCIETY, EYE, EAR, NOSE AND THROAT SECTION

Chairman: Dr. Maxwell D. Ryan, 660 Madison Ave., New York 21.
Secretary: Dr. Thomas H. Johnson, 30 W. 59th St., New York.

NORTH CAROLINA EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. A. J. Ellington, 412 S. Spring St., Burlington.
Secretary: Dr. J. A. Harrill, Bowman Gray School of Medicine, Winston-Salem.
Place: Hendersonville. Time: Sept. 16-19, 1946.

NORTH DAKOTA ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President: Dr. E. D. Perrin, 221–5th St., Bismarck.
Secretary-Treasurer: Dr. M. T. Lampert, Minot.

OREGON ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President: Dr. Wilfred Belnap, 833 S. W. 11th Ave., Portland.
Secretary-Treasurer: Dr. C. W. Kuhn, 1020 S. W. Taylor St., Portland 5.
Place: Good Samaritan Hospital, Portland. Time: Third Tuesday of each month.

PENNSYLVANIA ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. Thomas F. Furlong Jr., 36 Parking Plaza, Ardmore.
Secretary: Dr. Benjamin F. Souders, 143 N. 6th St., Reading.
Time: Last week in April.

RHODE ISLAND OPHTHALMOLOGICAL AND OTOLOGICAL SOCIETY

Acting President: Dr. N. Darrell Harvey, 112 Waterman St., Providence.
Secretary-Treasurer: Dr. Linley C. Happ, 124 Waterman St., Providence.
Place: Rhode Island Medical Society, Library, Providence. Time: 8:30 p. m., second Thursday in October, December, February and April.

SOUTH CAROLINA SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. J. H. Stokes, 125 W. Cheves St., Florence.
Secretary-Treasurer: Dr. Roderick Macdonald, 330 E. Main St., Rock Hill.
Place: Hendersonville, N. C. Time: Sept. 16-19, 1946.

TENNESSEE ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. George Burchfield, Maryville.
Secretary-Treasurer: Dr. Sam H. Sanders, 1089 Madison Ave., Memphis.

TEXAS OPHTHALMOLOGICAL AND OTO-LARYNGOLOGICAL SOCIETY

President: Dr. F. H. Rosebrough, 603 Navarro St., San Antonio.
Secretary: Dr. M. K. McCullough, 1717 Pacific Ave., Dallas.

UTAH OPHTHALMOLOGICAL SOCIETY

President: Dr. E. B. Fairbanks, 315 Medical Arts Bldg., Salt Lake City.
Secretary-Treasurer: Dr. Dean Spear, 516 Boston Bldg., Salt Lake City.
Place: University Club, Salt Lake City. Time: 7:00 p. m., third Monday of each month.

VIRGINIA SOCIETY OF OTO-LARYNGOLOGY AND OPHTHALMOLOGY

President: Dr. Thomas E. Hughes, 1000 W. Grace St., Richmond.
Secretary-Treasurer: Dr. Francis H. McGovern, 105 S. Union St., Danville.

WEST VIRGINIA STATE MEDICAL ASSOCIATION, EYE, EAR, NOSE AND THROAT SECTION

President: Dr. George Traugh, 309 Cleveland Ave., Fairmont.
Secretary: Dr. Welch England, 621½ Market St., Parkersburg.

LOCAL

AKRON ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. E. L. Mather, 39 S. Main St., Akron, Ohio.
Secretary-Treasurer: Dr. V. C. Malloy, 2d National Bank Bldg., Akron, Ohio.
Time: First Monday in January, March, May and November.

ATLANTA EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. B. M. Cline, 153 Peachtree St. N. E., Atlanta, Ga.
Secretary: Dr. Lester A. Brown, 815 Doctors Bldg., Atlanta, Ga.
Place: Academy of Medicine. Time: 7:30 p. m., fourth Monday of each month from October to May.

BALTIMORE MEDICAL SOCIETY, SECTION ON OPHTHALMOLOGY

Chairman: Dr. Jonas Friedenwald, 1212 Eutaw Pl., Baltimore.
Secretary: Dr. Fred Reese, 330 N. Charles St., Baltimore 1.
Place: Medical and Chirurgical Faculty, 1211 Cathedral St. Time: 8:30 p. m., fourth Thursday of each month from October to March.

Birmingham Eye, Ear, Nose and Throat Club

President: Each member, in alphabetical order.
Secretary: Dr. W. Chunn Parsons, 425 Woodward Bldg., Birmingham, Ala.
Place: Tutwiler Hotel. Time: 6:30 p. m., second Tuesday of each month, September to May, inclusive.

Brooklyn Ophthalmological Society

President: Dr. Benjamin C. Rosenthal, 140 New York Ave., Brooklyn.
Secretary-Treasurer: Dr. Louis Freimark, 256 Rochester Ave., Brooklyn 13.
Place: Kings County Medical Society Bldg., 1313 Bedford Ave. Time: Third Thursday in February, April, May, October and December.

Buffalo Ophthalmologic Club

President: Dr. William M. Howard, 389 Linwood Ave., Buffalo 9.
Secretary-Treasurer: Dr. Sheldon B. Freeman, 196 Linwood Ave., Buffalo 9.
Time: Second Thursday of each month from October to May.

Chattanooga Society of Ophthalmology and Otolaryngology

President: Each member, in alphabetical order.
Secretary: Dr. Douglas Chamberlain, Providence Bldg., Chattanooga, Tenn.
Place: Mountain City Club. Time: Second Thursday of each month from September to May.

Chicago Ophthalmological Society

President: Dr. W. A. Mann, 30 N. Michigan Ave., Chicago 2.
Secretary: Dr. J. R. Fitzgerald, 3215 W. North Ave., Chicago.
Place: Continental Hotel, 505 N. Michigan Ave. Time: Third Monday of each month from October to May.

Cincinnati General Hospital Ophthalmology Staff

Chairman: Dr. D. T. Vail, 441 Vine St., Cincinnati.
Secretary: Dr. A. A. Levin, 441 Vine St., Cincinnati.
Place: Cincinnati General Hospital. Time: 7:45 p. m., third Friday of each month except June, July and August.

Cleveland Ophthalmological Club

Chairman: Dr. M. Paul Motto, Rose Bldg., Cleveland.
Secretary: Dr. H. H. Wygand, 624 Guardian Bldg., Cleveland.
Time: Second Tuesday in October, December, February and April.

College of Physicians, Philadelphia, Section on Ophthalmology

Chairman: Dr. Burton Chance, 317 S. 15th St., Philadelphia.
Clerk: Dr. George F. J. Kelly, 37 S. 20th St., Philadelphia.
Time: Third Thursday of every month from October to April, inclusive.

Columbus Ophthalmological and Oto-Laryngological Society

Chairman: Dr. M. Goldberg, 328 E. State St., Columbus, Ohio.
Secretary-Treasurer: Dr. W. J. Miller, 21 E. State St., Columbus, Ohio.
Place: University Club. Time: 6:15 p. m., first Monday of each month, from October to May, inclusive.

Corpus Christi Eye, Ear, Nose and Throat Society

Chairman: Dr. L. W. O. Janssen, 710 Medical Professional Bldg., Corpus Christi, Texas.
Secretary: Dr. F. B. Kelly, 519 Medical Professional Bldg., Corpus Christi, Texas.
Time: 6:30 p. m., third Tuesday of each month from October to May.

Dallas Academy of Ophthalmology and Oto-Laryngology

President: Dr. Speight Jenkins, 1719 Pacific Ave., Dallas, Texas.
Secretary: Dr. L. Darrough, Dallas Medical and Surgical Clinics, Dallas, Texas.
Place: Dallas Athletic Club. Time: 6:30 p. m., first Tuesday of each month from October to June. The November, January and March meetings are devoted to clinical work.

Des Moines Academy of Ophthalmology and Otolaryngology

President: Dr. H. I. McPherrin, 406–6th Ave., Des Moines, Iowa.
Secretary-Treasurer: Dr. C. C. Jones, Bankers Trust Bldg., Des Moines, Iowa.
Time: 7:45 p. m., fourth Monday of every month from September to May.

Detroit Ophthalmological Club

Chairman: Members rotate alphabetically.
Secretary: Dr. Wesley G. Reid, 974 Fisher Bldg., Detroit 2.
Place: Club rooms of Wayne County Medical Society. Time: First Monday of each month, November to April, inclusive.

Detroit Ophthalmological Society

President: Dr. Bruce Fralick, 201 S. Main St., Ann Arbor, Mich.
Secretary: Dr. William S. Gonne, 619 David Whitney Bldg., Detroit 26.
Place: Club rooms of Wayne County Medical Society. Time: 6:30 p. m., third Thursday of each month from November to April, inclusive.

Eastern New York Eye, Ear, Nose and Throat Association

President: Dr. Frank C. Furlong, 713 Union St., Schenectady.
Secretary-Treasurer: Dr. E. Martin Freund, 762 Madison Ave., Albany.
Time: Third Wednesday in October, November, March, April, May and June.

Fort Worth Eye, Ear, Nose and Throat Society

President: Dr. C. R. Lees, 602 W. 10th St., Fort Worth 2, Texas.
Secretary-Treasurer: Dr. Van D. Rathgeber, 1305 Medical Arts Bldg., Fort Worth, Texas.
Place: Medical Hall, Medical Arts Bldg. Time: 7:30 p. m., first Friday of each month except July and August.

Houston Academy of Medicine, Ophthalmological and Oto-Laryngological Section

President: Dr. J. Matt Robison, 1304 Walker Ave., Houston, Texas.
Secretary: Dr. John H. Barrett, 1304 Walker Ave., Houston, Texas.
Place: River Oaks Country Club. Time: 6:30 p. m., second Thursday of each month from October to June.

Indianapolis Ophthalmological and Otolaryngological Society

President: Dr. J. Jerome Littell, 603 Hume Mansur Bldg., Indianapolis.
Secretary: Dr. J. Lawrence Sims, 23 E. Ohio St., Indianapolis.
Place: Indianapolis Athletic Club. Time: 6:30 p. m., second Thursday of each month from November to May.

Kansas City Society of Ophthalmology and Oto-Laryngology

President: Dr. Edgar Johnson, 906 Grand Ave., Kansas City, Mo.
Secretary: Dr. W. E. Keith, 1103 Grand Ave., Kansas City, Mo.
Time: Third Thursday of each month from October to June. The November, January and March meetings are devoted to clinical work.

Long Beach Eye, Ear, Nose and Throat Society

Chairman: Dr. Francis Carl Hertzog, 117 E. 8th St., Long Beach, Calif.
Secretary-Treasurer: Dr. Robert G. Thornburgh, 117 E. 8th St., Long Beach, Calif.
Place: Seaside Hospital. Time: Last Wednesday of each month from October to May.

Los Angeles Society of Ophthalmology and Otolaryngology

President: Dr. A. R. Robbins, 1930 Wilshire Blvd., Los Angeles.
Secretary-Treasurer: Dr. K. C. Brandenburg, 110 Pine Ave., Long Beach 2, Calif.
Place: Los Angeles County Medical Association Bldg., 1925 Wilshire Blvd. Time: 6:30 p. m., fourth Monday of each month from September to May, inclusive.

Louisville Eye and Ear Society

President: Dr. Joseph S. Heitger, Heyburn Bldg., Louisville, Ky.
Secretary-Treasurer: Dr. J. W. Fish, 321 W. Broadway, Louisville, Ky.
Place: Brown Hotel. Time: 6:30 p. m., second Thursday of each month from September to May, inclusive.

Lower Anthracite Eye, Ear, Nose and Throat Society

Chairman: Each member in alphabetical order.
Secretary: Dr. James J. Monohan, 31 S. Jardin St., Shenandoah, Pa.

Medical Society of the District of Columbia, Section of Ophthalmology and Otolaryngology

Chairman: Dr. P. S. Constantinople, 1835 I St. N. W., Washington.
Secretary: Dr. Frazier Williams, 1801 I St. N. W., Washington.
Place: 1718 M St. N. W. Time: 8 p. m., third Friday of each month from October to April, inclusive.

Memphis Society of Ophthalmology and Otolaryngology

Chairman: Each member, in alphabetical order.
Secretary: Dr. Sam H. Sanders, 1089 Madison Ave., Memphis, Tenn.
Place: Eye Clinic of Memphis Eye, Ear, Nose and Throat Hospital. Time: 8 p. m., second Tuesday of each month from September to May.

Milwaukee Oto-Ophthalmic Society

President: Dr. Ralph T. Rank, 238 W. Wisconsin Ave., Milwaukee.
Secretary-Treasurer: Dr. Frank G. Treskow, 411 E. Mason St., Milwaukee 2.
Place: University Club. Time: 6:30 p. m., fourth Tuesday of each month from October to May.

Montgomery County Medical Society

Chairman: Dr. H. V. Dutrow, 1040 Fidelity Medical Bldg., Dayton, Ohio.
Secretary-Treasurer: Dr. Maitland D. Place, 981 Reibold Bldg., Dayton, Ohio.
Place: Van Cleve Hotel. Time: 6:30 p. m., first Tuesday of each month from October to June, inclusive.

Montreal Ophthalmological Society

President: Dr. J. Rosenbaum, 1396 Ste. Catherine St. W., Montreal Canada.
Secretary: Dr. L. Tessier, 1230 St. Joseph Blvd. E., Montreal, Canada.
Time: Second Thursday of October, December, February and April.

Nashville Academy of Ophthalmology and Otolaryngology

Chairman: Dr. M. M. Cullom, 700 Church St., Nashville, Tenn.
Secretary: Dr. R. E. Sullivan, 432 Doctors Bldg., Nashville 3, Tenn.
Place: James Robertson Hotel. Time: 6:30 p. m., third Monday of each month from October to May.

NEW ORLEANS OPHTHALMOLOGICAL AND OTOLARYNGOLOGICAL SOCIETY

President Dr. W. B. Clark, 1012 American Bank Bldg., New Orleans.
Secretary: Dr. Mercer G. Lynch, 1018 Maison Blanche Bldg., New Orleans.
Place: Louisiana State University Medical Bldg. Time: 8 p. m., second Tuesday of each month from October to May.

NEW YORK ACADEMY OF MEDICINE, SECTION OF OPHTHALMOLOGY

Chairman: Dr. Brittain F. Payne, 17 E. 72d St., New York 21.
Secretary: Dr. Milton Berliner, 57 W. 57th St., New York.
Time: 8:30 p. m., third Monday of every month from October to May, inclusive.

NEW YORK SOCIETY FOR CLINICAL OPHTHALMOLOGY

President: Dr. Benjamin Friedman, 6 W. 77th St., New York.
Secretary: Dr. Benjamin Esterman, 983 Park Ave., New York 28.
Place: New York Academy of Medicine, 2 E. 103d St. Time: 8 p. m., first Monday of each month from October to May, inclusive.

OKLAHOMA CITY ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. S. R. Shaver, 117 N. Broadway, Oklahoma City.
Secretary: Dr. William Mussil, Medical Arts Bldg., Oklahoma City.
Place: University Hospital. Time: Second Tuesday of each month from September to May.

OMAHA AND COUNCIL BLUFFS OPHTHALMOLOGICAL AND OTO-LARYNGOLOGICAL SOCIETY

President: Dr. A. A. Steinberg, 1502 Farnam St., Omaha.
Secretary-Treasurer: Dr. W. Howard Morrison, 1500 Medical Arts Bldg., Omaha 2.
Place: Omaha Club, 20th and Douglas Sts., Omaha. Time: 6 p. m. dinner; 7 p. m. program; third Wednesday of each month from October to May.

PASSAIC-BERGEN OPHTHALMOLOGICAL CLUB

President: Dr. Thomas Sanfacon, 340 Park Ave., Paterson, N. J.
Secretary-Treasurer: Dr. J. Averbach, 435 Clifton Ave., Clifton, N. J.
Place: Paterson Eye and Ear Infirmary. Time: 9 p. m., last Friday of every month, except June, July and August.

PHILADELPHIA COUNTY MEDICAL SOCIETY, EYE SECTION

President: Dr. L. Waller Winckler, Philadelphia.
Secretary: Dr. Robert T. M. Donnelly, 255 S. 17th St., Philadelphia.
Time: First Thursday of each month from October to May.

PITTSBURGH OPHTHALMOLOGICAL SOCIETY

President: Dr. Jay G. Linn, Jenkins Arcade, Pittsburgh.
Secretary: Dr. Robert J. Billings, Jenkins Arcade, Pittsburgh.
Place: Pittsburgh Academy of Medicine Bldg. Time: Fourth Monday of each month, except June, July, August and September.

READING EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. Claude W. Bankes, 212 N. 6th St., Reading, Pa.
Secretary: Dr. Paul C. Craig, 232 N. 5th St., Reading, Pa.
Place: Wyomissing Club. Time: 6:30 p. m., third Wednesday of each month from September to July.

Richmond Eye, Ear, Nose and Throat Society

President: Dr. Luther C. Brawner, Professional Bldg., Richmond; Va.
Secretary: Dr. Clifford A. Folkes, Professional Bldg., Richmond, Va.
Place: Westmoreland Club. Time: 6 p. m., second Monday of each month from October to May.

Rochester Eye, Ear, Nose and Throat Society

President: Dr. Frank Barber, 75 S. Fitzhugh St., Rochester, N. Y.
Secretary-Treasurer: Dr. Charles T. Sullivan, 277 Alexander St., Rochester, N. Y.

St. Louis Ophthalmic Society

President: Dr. A. Lange, 3903a Olive St., St. Louis.
Secretary: Dr. William Kleinberg, Frisco Bldg., St. Louis.
Place: Oscar Johnson Institute. Time: Fourth Friday of each month from October to April, inclusive, except December, at 8:00 p. m.

San Antonio Ophthalmo-Oto-Laryngological Society

President: Dr. Belvin Pritchett, 705 E. Houston St., San Antonio 5, Texas.
Secretary-Treasurer: Lt. Col. John L. Matthews, AAF School of Aviation Medicine, Randolph Field, Texas.
Place: San Antonio, Brooke General Hospital, Randolph Field or San Antonio Aviation Cadet Center. Time: 7 p. m., second Tuesday of each month from October to May.

San Francisco County Medical Society, Section on Eye, Ear, Nose and Throat

Chairman: Dr. C. B. Cowan, 490 Post St., San Francisco.
Secretary: Dr. D. Harrington, 384 Post St., San Francisco.
Place: Society's Bldg., 2180 Washington St., San Francisco. Time: Fourth Tuesday of every month except June, July and December.

Shreveport Eye, Ear, Nose and Throat Society

President: Dr. David C. Swearingen, Slattery Bldg., Shreveport, La.
Secretary-Treasurer: Dr. Kenneth Jones, Medical Arts Bldg., Shreveport, La.
Place: Shreveport Charity Hospital. Time: 7:30 p. m., first Monday of every month except July, August and September.

Spokane Academy of Ophthalmology and Oto-Laryngology

President: Dr. Robert L. Pohl, W. 1104, 21st Ave., Spokane, Wash.
Secretary: Dr. Malcolm N. Wilmes, 407 Riverside Ave., Spokane, Wash.
Place: Spokane Medical Library. Time: 8 p. m., fourth Tuesday of each month except June, July and August.

Syracuse Eye, Ear, Nose and Throat Society

President: Dr. A. H. Rubenstein, 713 E. Genesee St., Syracuse, N. Y.
Secretary-Treasurer: Dr. I. H. Blaisdell, 713 E. Genesee St., Syracuse, N. Y.
Place: University Club. Time: First Tuesday of each month except June, July and August.

Toledo Eye, Ear, Nose and Throat Society

Chairman: Dr. W. W. Randolph, 1838 Parkwood Ave., Toledo 2, Ohio.
Secretary: Dr. John L. Roberts, 316 Michigan St., Toledo, Ohio.
Place: Toledo Club. Time: Each month except June, July and August.

Toronto Academy of Medicine, Section of Ophthalmology

Chairman: Dr. R. G. C. Kelly, 14 Lynwood Ave., Toronto 5, Canada.
Secretary: Dr. Alfred J. Elliot, 802 Medical Arts Bldg., Toronto 5, Canada.
Place: Academy of Medicine, 13 Queens Park. Time: First Monday of each month, November to April.

Washington, D. C., Ophthalmological Society

President: Dr. Harold M. Downey, 1740 M St. N. W., Washington, D. C.
Secretary-Treasurer: Dr. Richard W. Wilkinson, 1408 L St. N. W., Washington, D. C.
Place: Medical Society of District of Columbia Bldg., 1718 M St. N. W., Washington, D. C. Time: 7:30 p. m., first Monday in November, January, March and May.

Wilkes-Barre Ophthalmological Society

Chairman: Each member in turn.
Secretary: Dr. Samuel T. Buckman, 70 S. Franklin St., Wilkes-Barre, Pa.
Place: Office of chairman. Time: Last Tuesday of each month from October to May.